STUDIES OF SOME SYNTHETIC ASPECTS OF NON-STABILIZED AND STABILIZED SULFURANES

A THESIS

for the Degree of

DOCTOR OF PHILOSPHY

in

CHEMISTRY

Submitted to
BUNDELKHAND UNIVERSITY
JHANSI
1993

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My
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CERTIFICATE

Certified that the thesis entitled "STUDIES OF SOME SYNTHETIC ASPECTS OF NON STABILIZED AND STABILIZED SULFURANES", by Mr. Sanjeev Gupta, embodies the work carried out by him under my supervision. The work reported in the thesis is all original and has not been submitted elsewhere for the award of a degree Mr. Gupta has put in more than 200 days attendance in the laboratory during this work.

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ACKNOWLEDGEMENT

I deem it a pleasant duty and proud previlege to place on record my deepest sense of indebtedness to Dr. K.C. Gupta (M.Sc., Ph.D., F.I.C.S.) for introducing me to the field of ylide Chemistry and for his stimulating guidence and kind supervision throughout the course of this investigation.

I will be failing in my duty if I do not express my deep sense of gratitude to Dr. S.P. Saxena,Head, Chemistry Department of D.V.(P.G.) College, Orai for his inspiration, kind help and invaluable suggestions during the progress of my research work.

I wish to acknowledge my thanks to my teachers, Drs. A.K. Nigam, I.M. Beg, J.P. Pachauria, S.P. Srivastava, G.S. Niranjan, R.K. Nigam, S.K. Gupta, R.L. Viswarkarma and Mr. A.K. Srivastava for their encouragement.

I am also indebted to my colleauges, Messrs, Dr. P.K. Pathak, Dr. B.K. Saxena, Dr. A.K. Gupta, Dr. R.K. Gupta, Dr. U.C. Mishra, Dr. B.P. Pushpkar, Mr. Inayat Ali, Mr. Mohd.Masroor Beg for their active help during the course of this investigation.

My sincere thanks are due to Dr. G.S. Niranjan, Principal D.V.(P.G.) College, Orai for his encouragement and provision of laboratories facilities.

I am also thankful to the Director of C.D.R.I. Lucknow for providing facilities of spectral studies on a number of compounds.

I will always remain grateful to my elder Brother Mr. Rajeev Gupta, M.Tech., IIT Kanpur and loving younger sister Dr. Km.Rashmi Gupta, M.B.B.S. for giving their encourageful cooperation for completing my reaserch work.

I shall always obliged by Mr. Rajesh Kumar Gupta my colleage for making efficient typing of this thesis.

At last but not the least, I take the opportunity of expressing my deep gratitude to my parents to their encouragement and blessings at each & every stage of my carrier. Their kindness & understanding enabled me to traverse this difficult path, without their inspiration this present piece of work would have been quite impossible.

(SANJEEV GUPTA)

PLACE: ORAI

DATE : 1 Aug.,1993.

CONTENTS

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P R E F A C E

The thesis entitled "STUDIES OF SOME SYNTHETIC ASPECTS OF NON STABILIZED AND STABILIZED SULFURANES" has been divided into five chapters and each chapter describes specific aspects of ylide chemistry.

In chapter I, an exhaustive literature survey on π-sulfuranes leading to vast description about the types of non stabilized and stabilized sulfuranes. The chapter also contains the methods of prepration of stabilized and non stabilized sulfuranes and their some various important reaction.

Chapter II describes the reaction of benzyldimethyl sulfonium bromide and 4-nitrobenzyldimethylsulfonium bromide, 4-fluorobenzyldimethylsulfonium bromide, 4-bromodimethylsulfonium bromide with α, β-unsaturated ketones in presence of anhydrous $AlCl_3$ or $ZnCl_2$ at 150°C-200°C which is used for cyclization agent. The structures of these napthalene derivatives were confirmed by the elemental, IR and NMR spectral analysis.

In the chapter III gives an account of synthesis of new 2,4,6-triaryl substituted pyridines by the interaction of some 4-methoxyphenacyldimethylsulfonium bromide with α, β-unsaturated ketones in presence of a mixture of ammonium acetate and acetic acid. The structures of pyridines were confirmed by elemental, IR and NMR data.

In the chapter IV, various 2,4,6-tri substituted phenyl pyrimidines have been synthesized by the interaction of 4-nitrophenacyldimethylsulfurane and 4-fluorophenacyldimethyl sulfurane with aromatic aldehydes in presence of ammonium acetate and glacial acetic acid. Ammonium acetate in glacial acetic acid was used as aza cyclization agent.

The reaction takes place through Mannich type reaction. The methylene group of salt with aromatic aldehydes in presence of ammonium acetate forms Mannich base. Sulfonium salt which in turn, undergoes condensation with another molecule of benzaldehyde inpresence of ammonia to form sulfonium salt intermediate. The later, then undergoes elimination of dimethylsulfoniumhydrobromide to form 2,4,6-triarylpyrimidines.

Chapter V, includes the studies on metallation of six p-substituted phenacylidene dimethylsulfurane with $HgCl_2$, $HgBr_2$, $CdCl_2$, $CoCl_2$ and $NiCl_2$. The ylide carbanion coordinates with metal ions which is confirmed by $\nu C=O$ stretching vibrations of complexes. The structure of complexes were evidenced by IR spectral data and elemental analysis.

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CHAPTER I

CHAPTER - I

STUDIES OF SOME SYNTHETIC ASPECTS OF NON STABILIZED AND STABILIZED SULFURANES

A GENERAL SURVEY :

Ylide (1) are a new and unique class of zwitterionic compound in which carbanion is covalently linked to a positively charged heteroatom. Its structure is considered resonance hybrid of two limiting structures - Ylide forms (1a) and ylene form (1b) One of these, the ylide form (1a) emphasizes the dipolar zwitterionic nature involving an onium centre at elements like nitrogen, phosphorous or arsenic, next to a carbanionic function which may atleast be partially delocalized into suitable substituents. In t ylene form (1b), on the other hand, a true double bond is postula ted between the centre and ylidic carbon, thus reducing or even eliminating the formal charges at these atoms[1-2]. The application of modern physical techqniques and the results of sophisticated theoritical calculations[3-5], have made it increasingly clear that the ylide form predominates in the ground state. Most of the early investigations successfully used description for most of their problems of structure and reactivity and for the rationalization of reaction mechanism[2-6]. Therefore, it is with justification that the term ylide is used now a days almost exclusively in the literature.

The reactivity of the ylides depends both upon the

properties of the carbanion and on the possible involvement of the heteroatom. These compounds vary widely in stability, depending upon the symmetry of the molecule and the extent of $p_{\pi} - d_{\pi}$ bonding.

A quantitative comparison of the stability of ylides, formed by different elements, have been made using the rates of alkali catalyzed exchange[7] of the α-hydrogen atoms of the corresponding salts. The acidity of salt and hence the stability of the ylide is greatly affected by the change in structure.

Ylide have been classified in two main groups on the basis of stability and ease with which they undergo reaction with a variety of electrophillic substrates. The first and the larger group comprises of ylides, called "non-stabilized ylides". Which are generated in the solution from their corresponding salts but could not be isolated due to the stabilizing factors and undergo reaction in situ. These ylides may further be divided in two catagories depending upon the attachment of alkyl or arylalkyl groups with the heteroatom. The arylalkylidene ylides, sometimes designated as semi-stabilized ylides which could not be isolated but persisted in solution for a considerable time, in contrast to the alkylidene ylides which are very short-lived. The second and the smaller group consists of "stabilized ylides"

and is taken to imply an ylide which can be isolated, purified, usually stored in atmosphere and used in subsequent reactions. The stability of these ylides is attributed to the attachment of the electron withdrawing groups with the ylidic carbanion. In the recent years, the synthetic potentialities of ylides have been realized and studies on these reactive intermediates have been expanded in many directions which lead to the exploration of the ylides of nitrogen, phosphorous, arsenic and sulfur as evidenced by the research monographs[6-11,8-12] and comprehensive review articles[12-25]. The involvement of a particular heteroatom results into marked difference in the chemical and physical behaviour of different types of ylides.

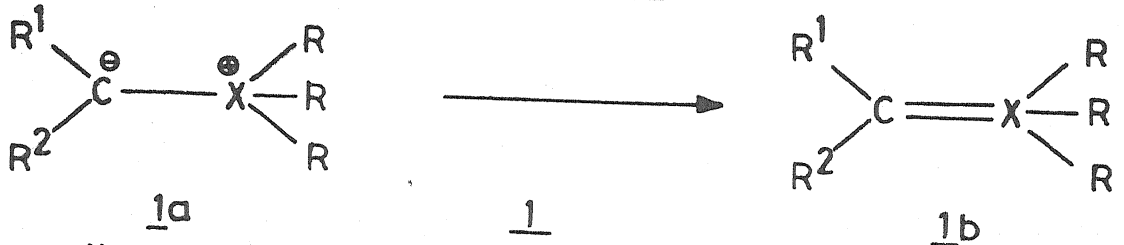
The scope and potential for synthetic applications of these ylides has only recently been realized. Consequently, studies on pyridinium, phosphonium, arsonium and sulfonium ylides and their corresponding precursors have been very extensive. These investigations have lead to the synthesis of a wide variety of heterolytic compounds, vitamins, hormones etc.as evidenced by a large number of monographs[6-11] and comprehensive review articles[12-25]. A brief description under separate heads has been reviewed in the following section.

Ingold and Jessop's [26] earlier investigations gave the synthetic chemistry of S-ylides in 1930. His success was the isolation of a stabilized π-sulfuranes, a fluorenylidene

dimethyl sulfuranes (3) by reactivity 9-fluorenyl-dimethyl sulfonium bromide (2) with aquous Na_2CO_3 (Scheme I.1). This class of compounds could not get the success regarding their reactivity and synthetic potentialities in the litrature it showed an isolated event. But in the early sixtees a flury of activities when G. Wittig[27], isolated successfully and studies the reactivity of p-ylides towards carbonyl compounds. It was his concluding fact that any molecular system capable of providing adequate stabilization to a carbanion may form an ylide[28] system and prompted from Wittig investigation in the p-ylide chemistry. An active interest revived by Jhonson and Lacount[29] when they isolated fluorenylidene dimethyl sulfurane (3) successfully. Reactivity of the some ylide (3) having the fact that the ylide afforded sufficient stabilization due to delocalisation of the lone pair of electron present on the ylide carbanion as shown by resonating structures (3 a,b,c) and therefore prevented the ylide (3) from being entered into reaction electrophillic substrate could not be studied too by them. With benzaldehyde the reaction of ylide (3), form 9-benzalfluorene was failed because it provided benzalfluorene oxide (5) and phenyl -9 (methythiomethyl) fluorenyl carbinols(6) in the place of benzal fluorene (Scheme I.2).

In connection the same Corey and Chaykovsky[30] reported reactions of the prepration more reactive and a less stable ylide methylenedimethyl oxosulfonium ylide (7). Having the

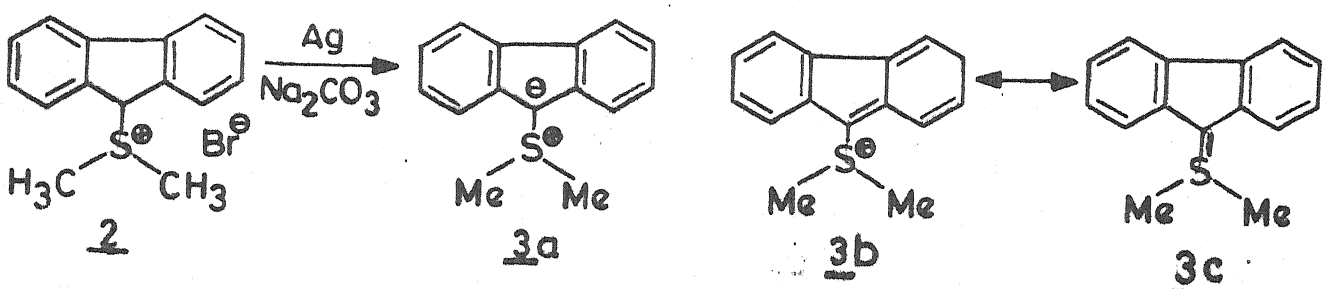
Schemes



1a 1 1b

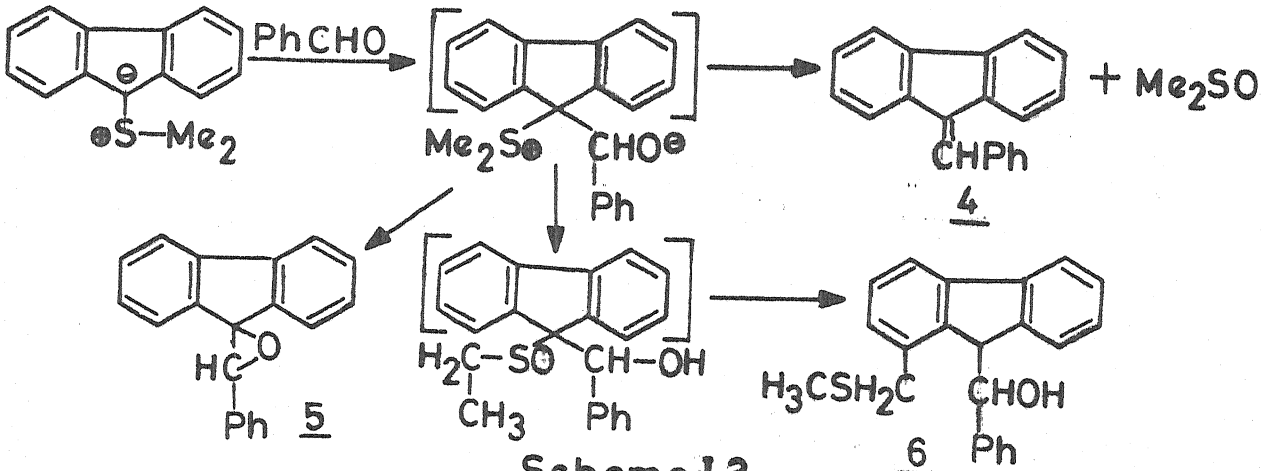
(where X may be N, P, As, S etc.)

Scheme 1.1



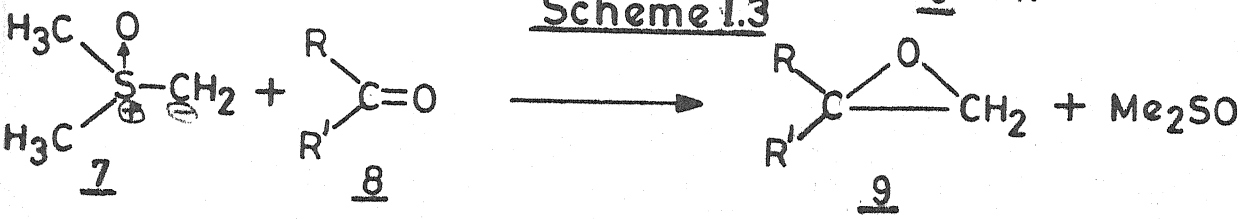
2 3a 3b 3c

Scheme 1.2



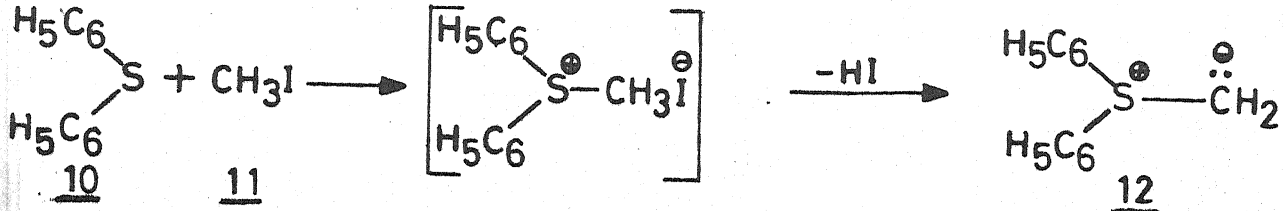
4 5 6

Scheme 1.3



7 8 9

Scheme 1.4



10 11 12

ability of P-ylides to act as a good carbonyl olefinating reagent[27] Corey et al[31] have also tried to react oxosulfonium ylide (7) with aldehydes and Ketones (8) and assumed to get the olefins but failed because the exclusive products were epoxides (9) (Scheme I.3).

In accordance with these observations oxosulfonium ylides were known as a versatile status of epoxidation reagents. Now an exclusive efforts were made to explore the synthetic potentialities of these ylides.

After this Franzen and Driessen[32] made a successfull attempt to synthesize a new kind of π-sulfuranes so called sulfonium ylides (12). Through the interaction of methyl phenyl sulfide (10) with methyl iodide (11) followed by Dehydrohalogenation (Scheme I.4). In comparison to oxosulfonium ylide (7), the ylide (12) so formed was less stable. This has been represented by the fact that the ylide gets decomposed in the absence of suitable substrates.

In the subsequent years Corey and Chaykovsky[33] have reported that sulfonium ylides undergo not only methylene transfer reaction on carbonyl group to form epoxides but also add on C=C, having some unsaturated groups in conjugation to form cyclopropanes. So methylene dimethyl sulfurane identified itself as appropriate epoxidation reagent to provide oxirane(13). Oxosulfonium methylide has capabilities to add on to activated

C=C to form cyclopropanes (14). Thus undoubtlly π-sulfuranes are the best methylene transfer agents (Scheme I.5)[34]. Incoming years, the synthetic potentialities of π-sulfuranes have further been realized and illustrated in many ways with a view to test the domain of the applicability of these ylide systems as evidenced by recent monographs several comprehensive review articles[35-41].

A type of classes of π-sulfuranes are known the most common being sulfonium ylide (15), oxosulfonium ylide (16), sulfenyl ylides (17), sulfinyl ylides (18) and ~~innuno~~ imino sulfuranes (19).

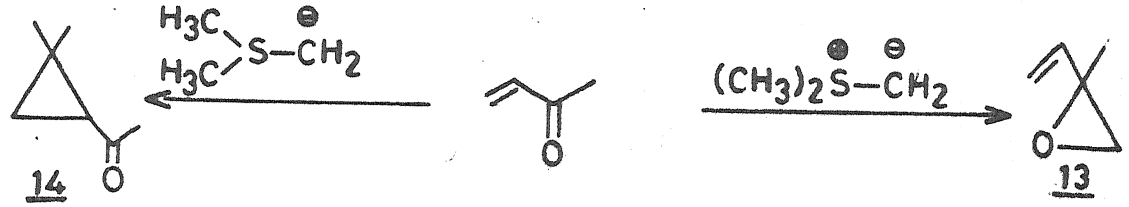
The stability of π-sulfuranes may be attributed to the electrostatic stabilization as well as delocalization of charge on the ylidic carbanion with d-orbitals of S-atom[42-43]. The magnitude of electrolytic stabilization of π-sulfuranes is completly controlled by the magnitude of charges present on the onium group as well as on the carbon ylide. Illustrating to this fact it can be observed that oxosulfonium ylides are more stable than their sulfonium counter parts, having to the increased positive charge on the S-atom due to the presence of more electronegative oxygen atom. The another factor which also makes a notable contribution to the stability of π-sulfuranes (20) is delocalization involving the use of 3d-orbitals which is the maximum. If the sulfur atom carries a full unit of(+ve)

charge. The overlapping of doubly occupied 2p-orbital of the ylide carbon with the formation of π-bond while the lone pair on S-remains in a 3p-orbital. This can be represented in the resonance hybrid of two limiting structures, the ylide form (20a) and the ylene form (20b). These factors are sufficient enough to explain as to why a series of π-sulfuranes have been isolated a charecterized as stable species. Further more the maximum overlap of a 2p-carbon orbital (21a) with a 3d-orbital of S-atom is reported only when the molecule had the tendency to become coplaner (21b) & can be represented by $p_{\pi} - d_{\pi}$ orbital overlap structure (21).

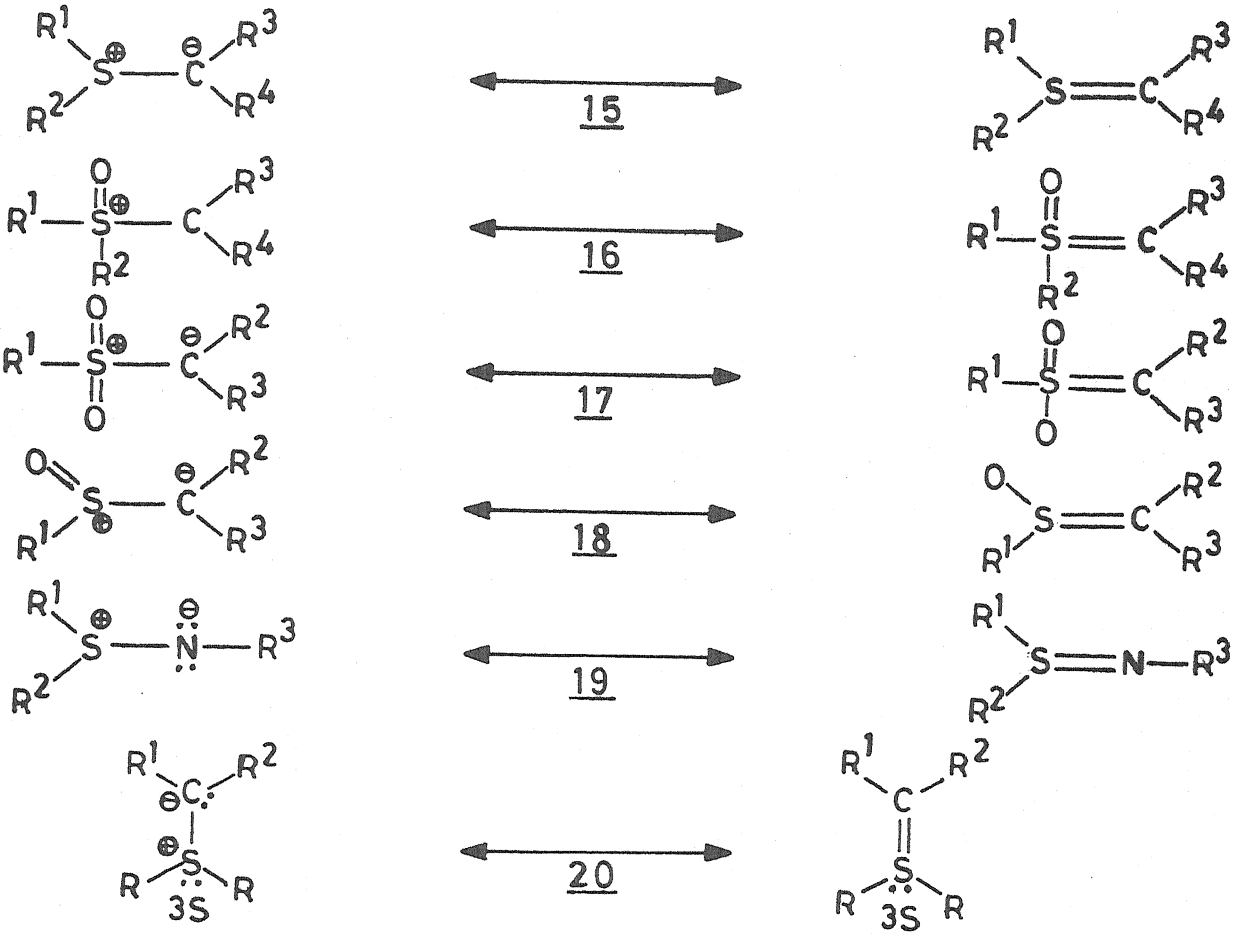
However from recent ESCA data it has been concluded that the stability of these ylides is also influenced by the presence of certain electronegative groups on the ylide carbon. The reason is that the formal (-ve) charge on the ylide carbon actually, highly delocalization into substitution attached by the ylide carbon (22).

The reactivity of π-sulfuranes depends on the properties of the carbanion as well as the possible involvement of the heteroatom[33,44-53]. Usually alkylidene sulfuranes of less stability show high reactivity whereas highly stabilized alkylidene sulfuranes is show less reactivity. The reactivity of alkylidene sulfuranes is influenced by the distribution of the (-)ve charge over the molecule which, in turn, depends

Scheme 1.5



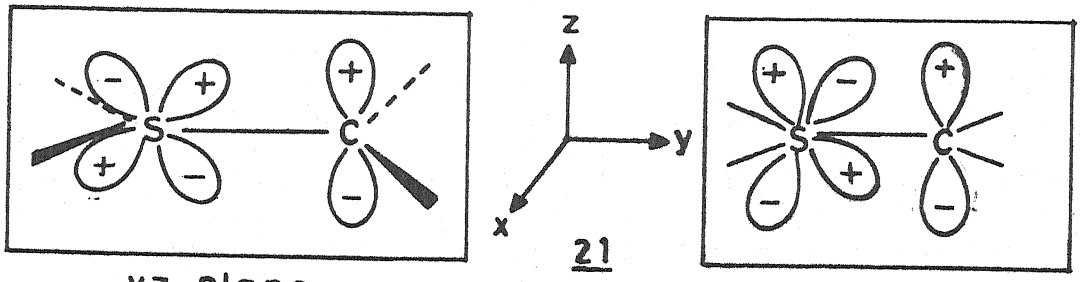
14 13



15 16 17 18 19 20

20 a

20 b



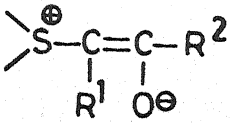
yz plane

21 a

21

xy plane

21 b



22

on the nature of the substituents R^1 and R^2 in the alkylidene position as well as on the group R on sulfur. Thus the nucleophilic charecter of the sulfurane decreases if the lone pair of electron on the α-carbon atom of the form (20a) is delocalized into group R^1 and R^2 tend to stabilize the (-)ve charge and consequently reduce the reactivity of the ylides.

On the otherhand, when there is no such interaction, an extremly reactive and unstable π-sulfurane is formed.

Prompted from the enhanced reactivity and easy prepration of the π-sulfuranes, it was to be thought of interest to focus our attention on synthesizing some new sulfonium ylides with a view to test their reactivity towards a variety of electrophillic substrates, resulting into the formation of diverse carbocyclic and heterocyclic systems[54-57].

I.1. PREPRATION OF π-SULFURANES VIZ. SULFONIUM YLIDES :

I.1.1. π-Sulfuranes from sulfonium salt :

This remains the most common method of generating π-sulfuranes and involves the reactions of sulfonium salt with a base which is strong enough to obstruct proton from α-carbon. In principle, any sulfonium salt (23) carrying at least one α-hydrogen in convertible into an ylide (24) (Scheme I.6). In practice the salt method is applicable only for three structural situations. In the first instance, all the

three of the groups attached to the S-atom must be identical so that it makes no difference which α-hydrogen removed by the base. In the second instance one or the two of the substituents have no α-hydrogen but these groups which do are identical[32]. The first and the last structural situation in which the sulfonium salt method[26-54] is applicable necessitable there being an appreciable difference in the acidity of various available α-hydrogens and the availability of a base of the proper strength. The deprotonation of the more acidic α-hydrogen is always preferred. If the sulfonium salt (25) possesses three different kind of α-hydrogen and each of approximately the same acidity, then a mixture of π-sulfuranes results (Scheme I.7)

Numerous bases have been employed for the generation π-sulfuranes and the strength of base to be used depends on the acidity of the sulfonium salts. Thus trialkyl sulfonium salts required very strong bases such as methyl lithum[55], potassium-t-butoxide[29,56] in dimethyl sulfoxide or methyl sulphinyl carbanion[32-33]., Further literature survey revealed that in the generation of stabilized π-sulfuranes only relatively weak bases such as trimethylamine, aq.NH_3 or aq.NaOH[57] are respectively required. Also solvents such as dimethyl sulfoxide or tetrahydrofurane are reported to be used for the non stabilized π-sulfuranes[58]. Protic organic solvents or water have been shown to react with the non stabilized π-sulfuranes and therefore these solvents have not been employed

for their generation[59-61] of π-sulfuranes.

I.1.2. π-Sulfuranes from benzyene and organic sulfides :

Among few other methods employed for the generation of π-sulfuranes are involving the reaction of dialkyl sulfides (29) with benzyne (30) is used for generation of such π-sulfuranes (ylides) (31). In which S-atom of the ylide carried one phenyl ring[66]. But in practice, this method is of little importance. Because the presence of phenyl ring in resulting ylide renders them less reactive due to delocalization of the (+)ve charge carried by S-over phenyl ring (Scheme I.8).

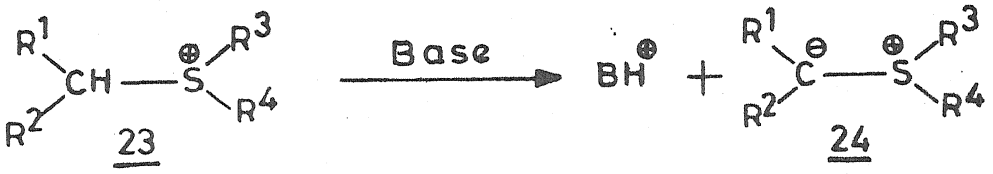
I.1.3. π-Sulfuranes via alkylation and acylation method :

A wide variety of complex which are quite inaccessible by the conventional salt method have been prepared by the method called alkylation[67] or acylation[68]. The method involves the interaction of the simple ylides with alkylating or acylating reagent to form more substituted stabilized ylides (Scheme I.9).

I.1.4. π-Sulfuranes from active methylene compound and sulfoxides :

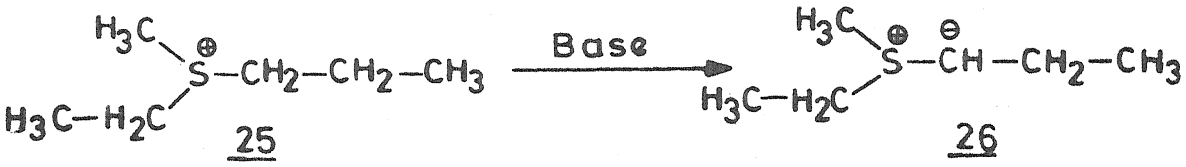
The condensation of active methylene group (33) with sulfoxides or alkoxy sulfonium salts (32) offers a direct-route for the synthesis of highly stabilized ylide (34) via intermediate salt formation[69-71](Scheme I.10).

Scheme 1.6



23 24

Scheme 1.7



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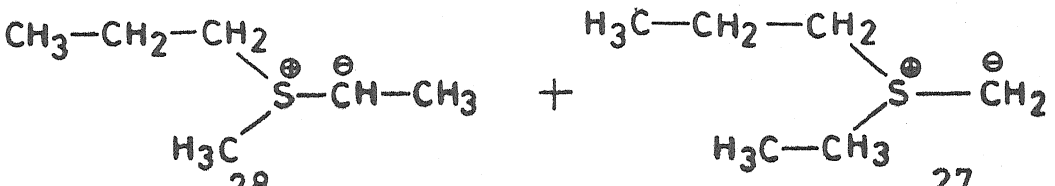
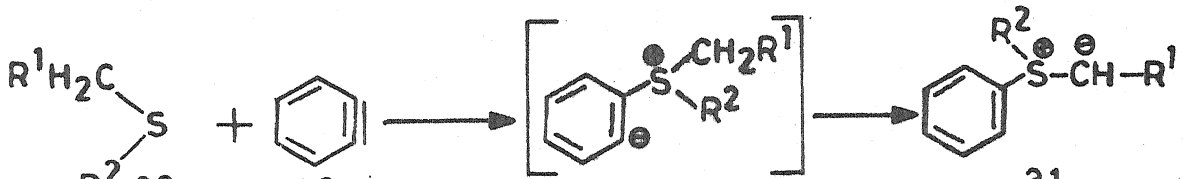


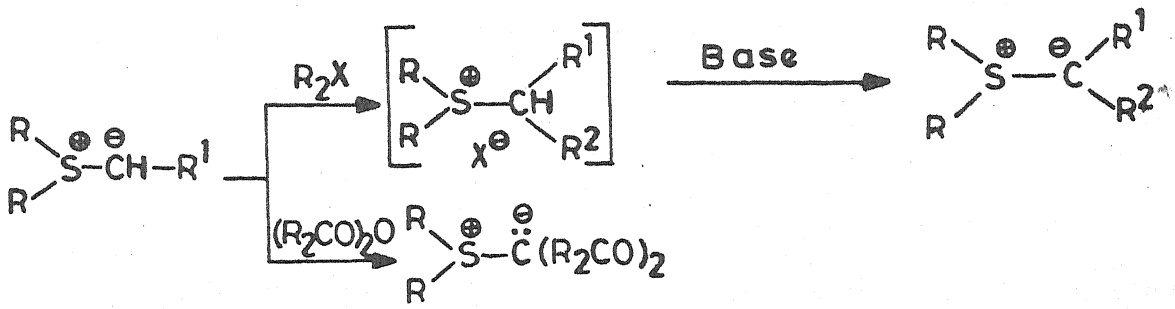
28 27

Scheme 1.8

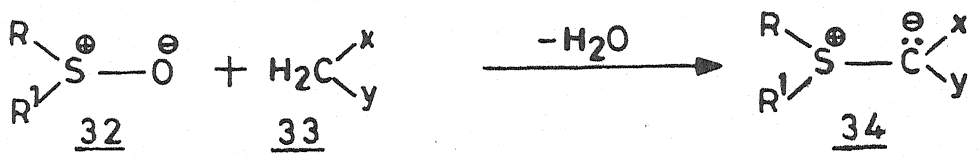


29 30 31

Scheme 1.9

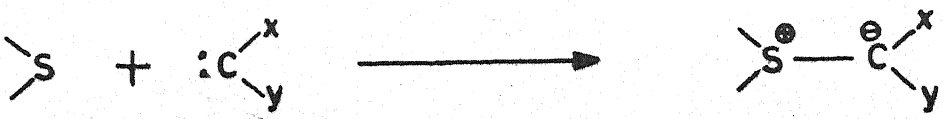


Scheme 1.10



32 33 34

Scheme 1.11



The reaction with sulfoxides is favoured in presence of dehydrating agents. In general acetic anhydride, phosphorous pent oxide, phenyl isocyanate and dicyclohexyl carbo di-imide-phosphoric acid are highly suitable for bringing about the desired results.

I.1.5. π-Sulfuranes from carbenes :

The addition of to a sulfide provides a most direct synthesis of π-sulfuranes (Scheme I.11)[72-74] Diazo compounds serve as the good source of carbene intermediate for the prepration of ylides (37). The copper catalyzed thermal or photolytic decomposition of diazo compounds (36) in presence of an allyl or benzyl sulfide (35) appears to be the most attractive synthetic technique (Scheme I.12). However it was observed that thermal decomposition of diazo compounds is more suitable for synthesizing ylides.

I.1.6. π-Sulfuranes via Michael addition to vinyl sulfonium salt :

The Michael addition to a vinyl sulfonium salt (38) also produces π-sulfuranes[75-76] (Scheme I.13). The resulting ylide (39), if stable is isolable and can be trapped by the attack of suitable reagents or it can further react intermolecularly.

I.1.7. π- Sulfurane from electrochemical reduction of sulfonium salts :

Only one example relating to the prepration of ylide (41) by this method is given in the literature[77], which involves the reduction of trimethyl sulfonium salt (40) in DMSO solution (Scheme I.14).

I.1.8. π- Sulfuranes from other methods :

Dimethyl sulfonium methylide is capable of being prepared in good yields by the phase transfer catalysis[78]. A ligand exchange reaction between triphenyl sulfonium cation and cyclopropyl lithium gives diphenyl sulfonium cyclopropylide[79] in good yields. The synthesis of Thiaranes[80] and an asymmetric synthesis Thiaranes[81] by the reaction of aldehydes and ketones with S-lithiomethyl-O-(-)methyl dithiocarbonate have been reported recently.

I.2. REACTIONS OF π-SULFURANES :

I.2.1. Phenacyl dimethyl sulfonium bromide (with halogen acids) :

Ratt's et al[57] have reported that phenacylidene-dimethyl ylide on its reaction with HBr acid affords dimethyl phenacyl sulfonium bromide. Jhonson et al[68] tested the reaction and demonstrated that almost all the carbonyl stabilized sulfonium[42] ylides reacts with hydrogen bromide (43) to form

conjugate acid (44) of the ylide (42)(Scheme I.15). These observations clearly indicate that sulfonium ylides are nothing but the conjugate bases of dimethylphenacyl sulfonium bromide.

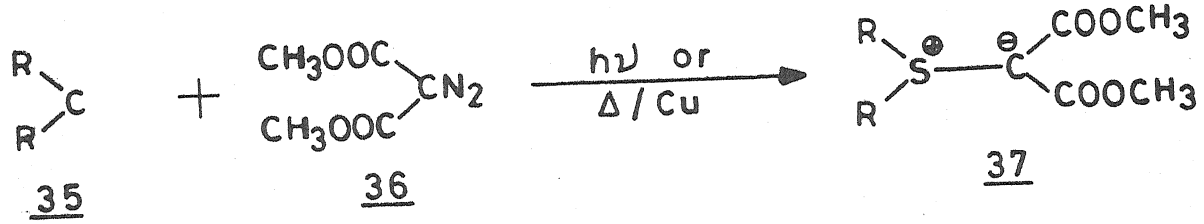
I.2.2. Thermolysis of π-sulfuranes :

The existing literature lacks in sufficient information concerning the thermolysis of sulfonium ylides. However Jhonson et al[70] have shown that the non stabilized sulfonium ylide, diphenyl sulfonium benzylide (45), on thermolysis dissociates into carbenes (46) and phenylsulfide (47) (Scheme I.16). On the otherhand, thermolysis of stabilized ylide, phenacylidene dimethyl sulfurane (48), takes different course[82-83] where carbene generated by the thermal dissociation of the ylide dimerises to form dibenzoylethylene which, in turn, is attacked by one mole of the original ylide (48) affording 1,2,3-Tribenzoyl-cyclopropane (49) through carbenoid mechanism (Scheme I.17).

I.2.3. Photolysis of π-sulfuranes :

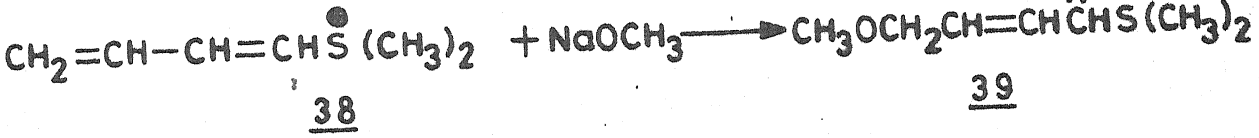
Photolytic conversion of the π-sulfuranes has been less studied. However Trost et al[84] have reported that photochemical decomposition of diphenyl sulfonium allylide (50) occurs in which cyclopropane (51) is isolated in 25% yields (Scheme I.18). Subsequent to this Corey and Chaykvsky[85] developed an Arndt- Eistert type of process to yield esters (54) by irradaiation of β-keto-oxosulfonium ylide (53) prepared

Scheme I.12



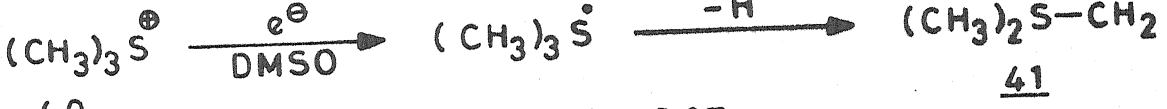
35 36 37

Scheme I.13



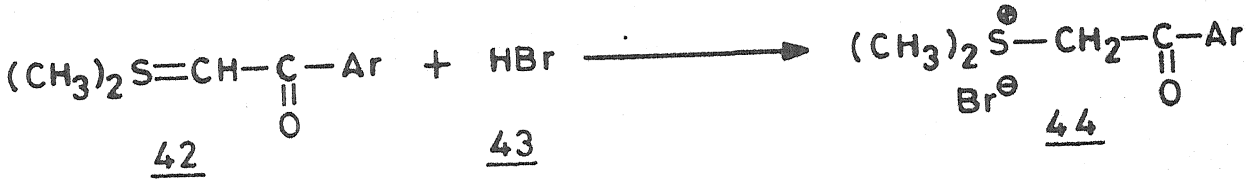
38 39

Scheme I.14



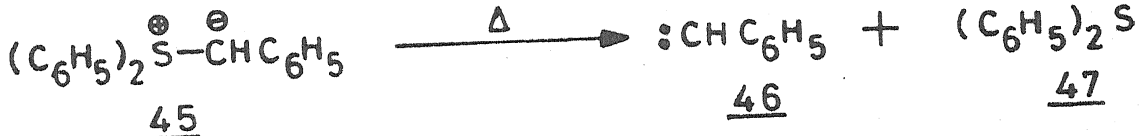
40 41

Scheme I.15



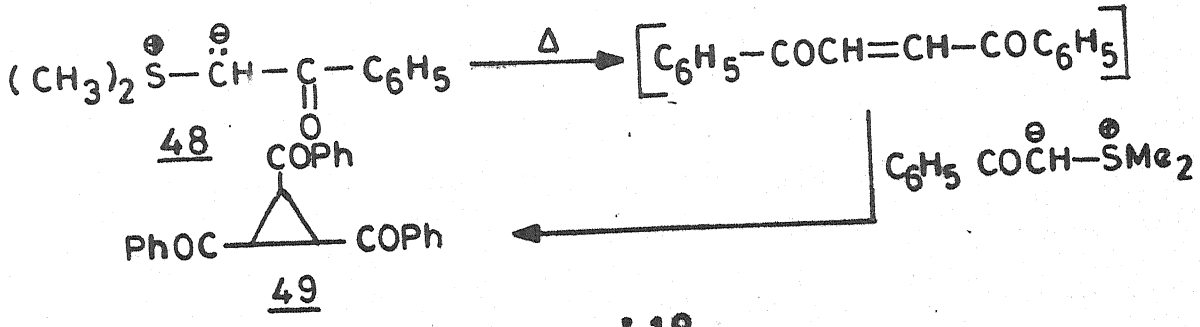
42 43 44

Scheme I.16



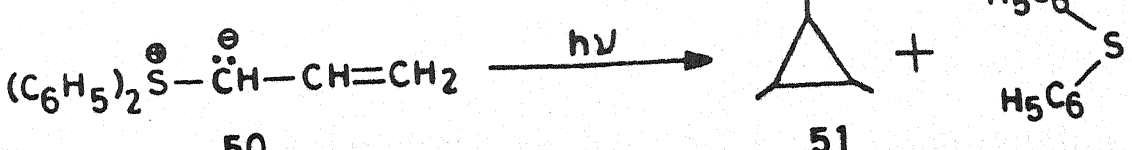
45 46 47

Scheme I.17



48 49

Scheme I.18



50 51

by acylation of methylide (52) (Scheme I.19).

I.2.4. Tribenzoyl cyclopropane(with α-bromo ketones):

Jhonson et al[86] have reported that the phenacylidine dimethyl sulfurane (55) reacts either with its conjugated acid (56) or phenacyl bromide (57) to afford tribenzoyl cyclopropane (58). The mechanism of the reaction appears to involve an acylation elimination addition sequence(Scheme I.20).

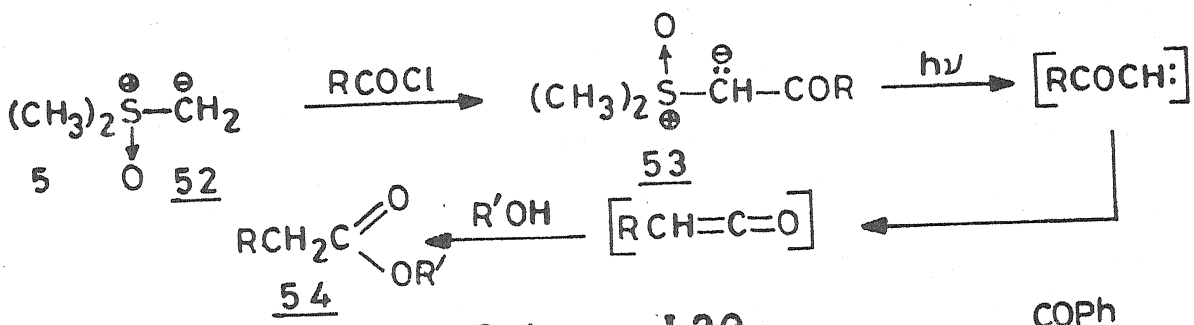
I.2.5. Alkylation of π-sulfuranes :

The alkylation reactions have assumed importance because of their ability to offer a versatile route for synthesis of disubstituted ylides which are otherwise difficult to prepare. Other route Jhonson et al[68] studied the alkylation of phenacylidine dimethyl sulfurane (59) with benzyl bromide(60) where α-methyl-thio- β-phenyl propiophenone (61) was reported to have been formed (Scheme I.21).

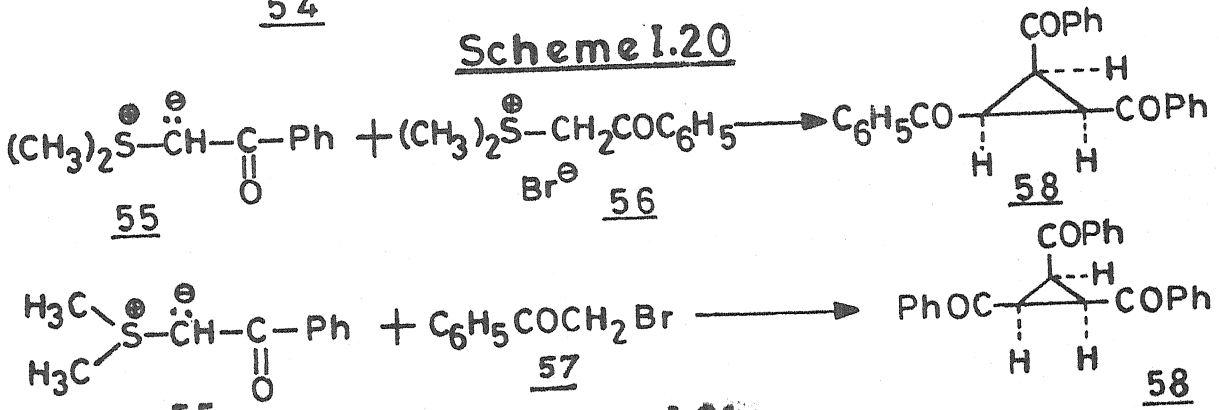
I.2.6. Acylation of π-sulfuranes :

Based on information gathered so far non stabilized π-sulfuranes are not liable to be attacked by acylating reagents. However stabilized π-sulfuranes are reported to undergo acylation reaction with a couple of acylating reagents[68-8] and it is observed that the course of acylation depends on the nature of the acylating reagents. Thus phenacylidenedimethyl-sulfurane (62) on reaction with benzoic anhydride undergoes

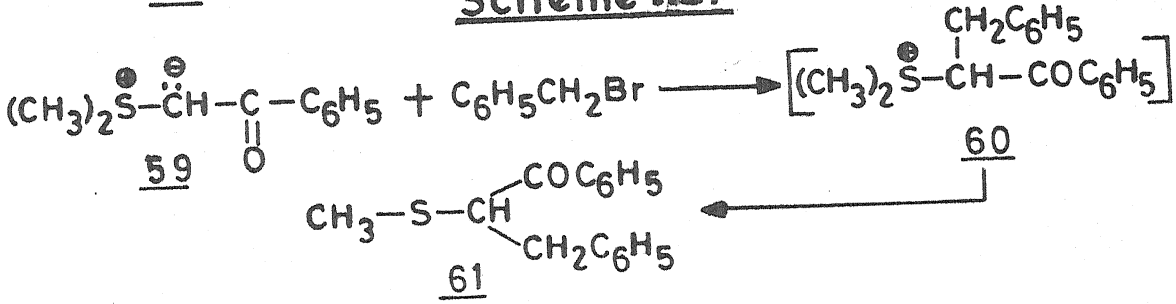
Scheme I.19



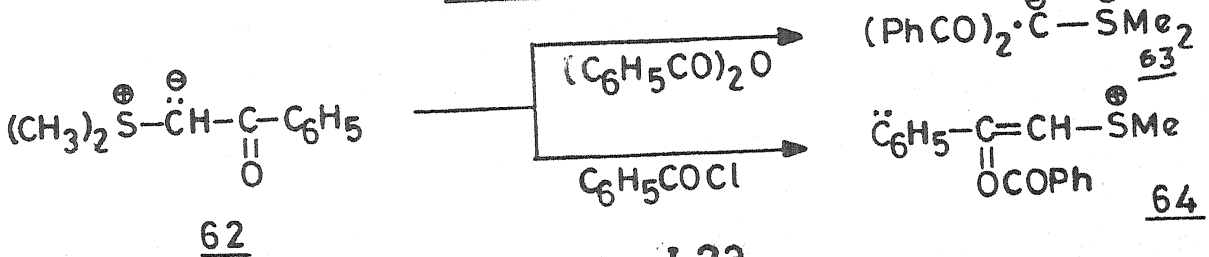
Scheme I.20



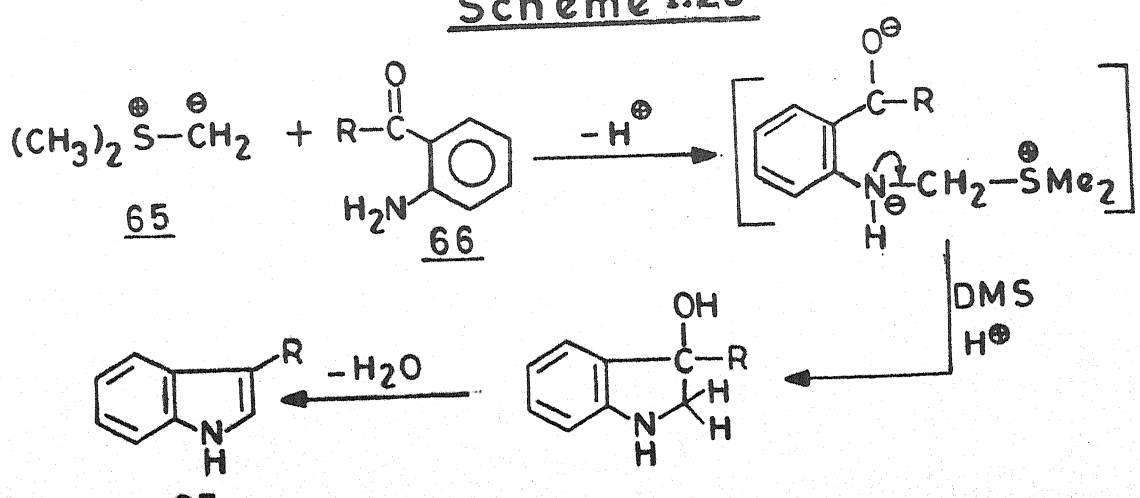
Scheme I.21



Scheme I.22



Scheme I.23



C-alkylation to afford a new ylide (63). On the otherhand ylide (62) follows O-acylation when treated with benzoyl chloride, thus affording enol benzoate(64) (Scheme I.22).

I.2.7. Synthesis of Indoles : (Reaction with amino compounds)

Bravo and his cowerkers[88] have synthesised a wide variety of substituted indoles (67) by the reaction of dimethyl sulfonium methylide (65) with aromatic-o-amino carbonyl compounds (66) (Scheme I.23). Later on Junjappa[35] reported the formation of 2-substituted indoles (70) by the interaction of carbonyl stabilizedsulfuranephenacylidene dimethyl sulfurane (68) and substituted anilines (69) in the presence of diethylaniline (Scheme I.24).

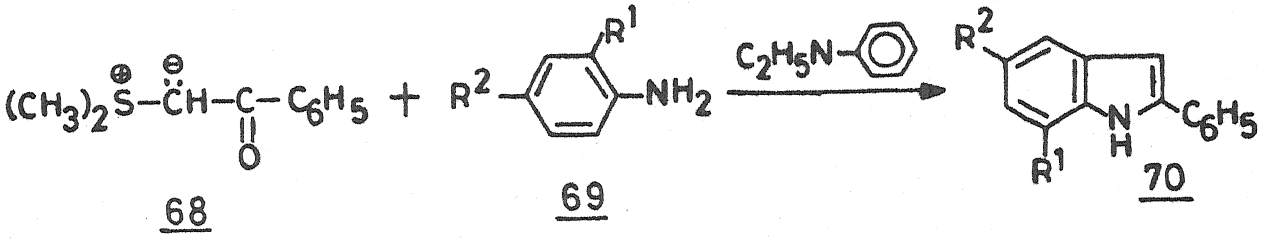
I.2.8. Benzothiophens (Reaction with mercapto compound):

Bravo et al[89] have demonstrated that dimethyl sulfonium methylide (72) is capable of undergoing reactions with o-mercapto ketones (71) forming benzothiophenes (73) (Scheme I.25).

I.2.9. Pyrazole derivatives (Reaction with nitrile amine):

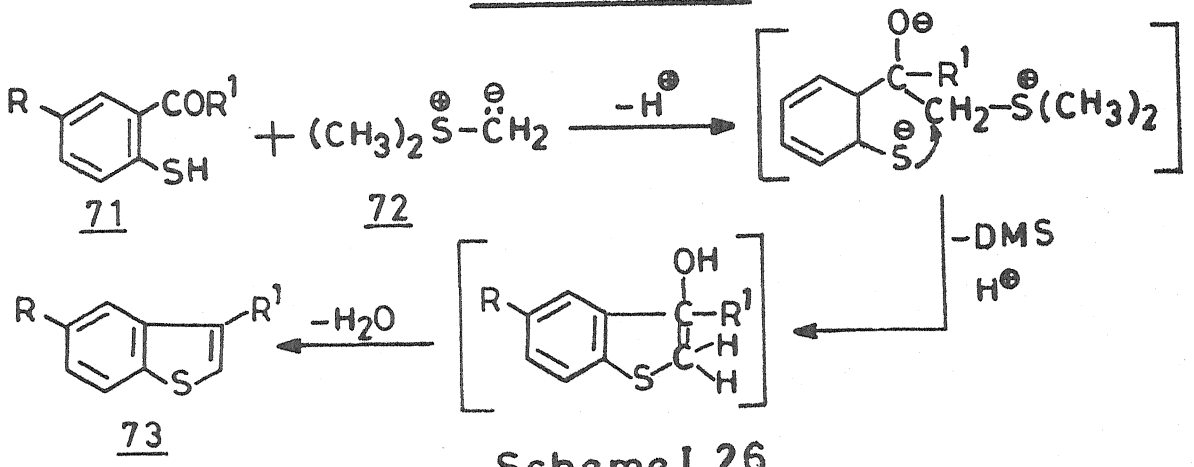
The carbonyl stabilized sulfonium ylides have also been reported in literature[90] to undergo reaction with nitrimines affording pyrazole derivatives. For example, the reaction of stabilized sulfuranes (74) with N-(α-chlorobenzylidene)

Scheme I.24



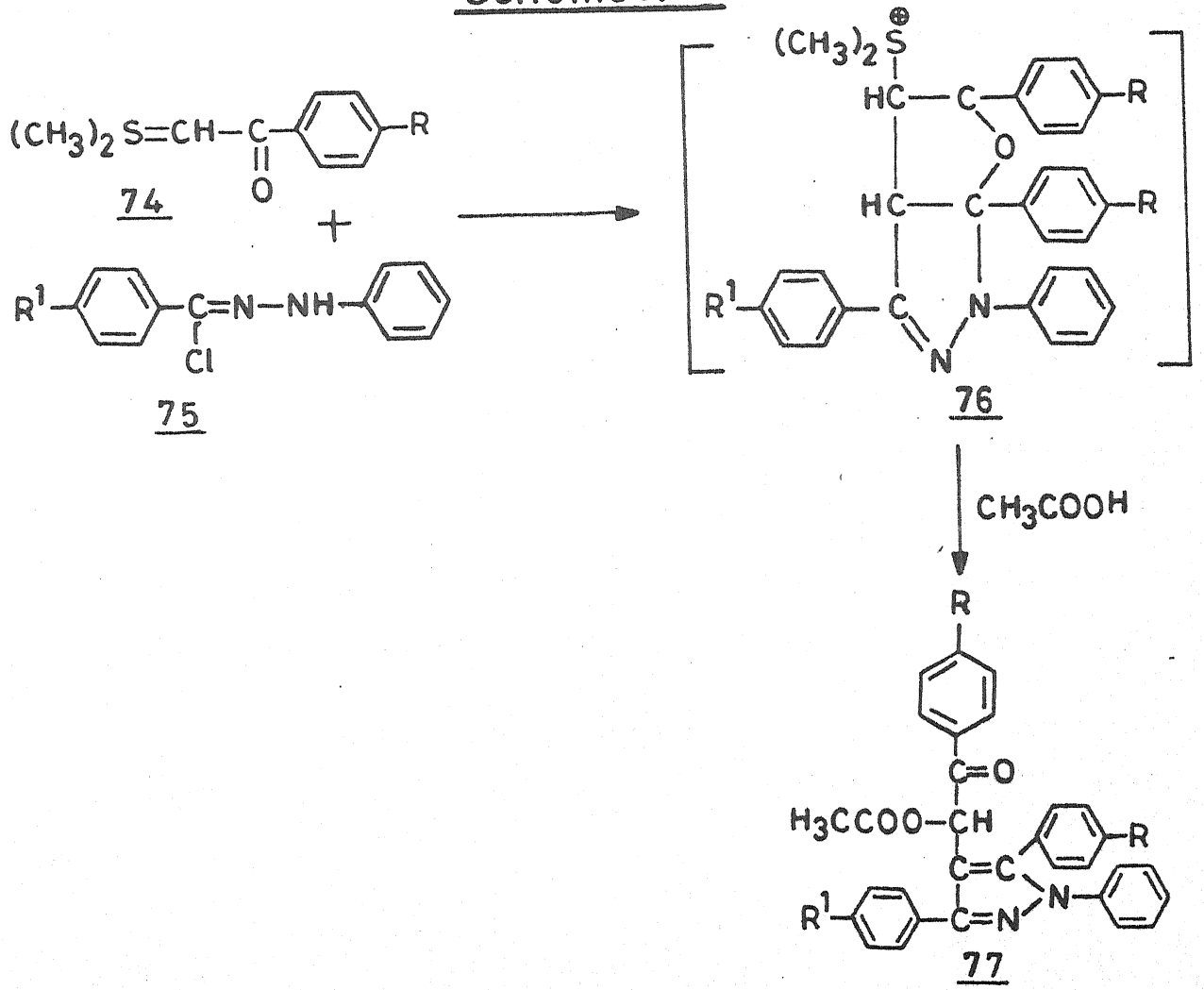
68 69 70

Scheme I.25



71 72 73

Scheme I.26



74 75 76 77

N-phenyl hydrazine (75) affords pyrazole (77) via intermediacy of the cyclic products (76). This reaction has assumed big importance in the synthesis of pyrazole derivatives (Scheme I.26).

I.2.10. With multiple bonds :

2.10.1. With C-O double bonds :

The best known reaction of sulfonium ylides which attained importance in the preprative organic chemistry under the name of epoxidation involves the combination of these ylides (78) with carbonyl compounds (79) to form oxiranes (81) exclusively. The reaction proceed via the intermediacy of betaine type of compound (80) formed by the nucleophillic attack of the ylidic carbonium on the carbonyl carbon atom and involving displacement by the oxyanion on the carbon carrying the onium group. It appears[91] in the case of sulfonium betaine (80) that the potential S-O bond formation is not a sufficient driving force to dictate the course of the reaction (Scheme I.27). The conjugation and stabilization afforded by the substituents (R^1) present on the ylide as well as on the carbonyl group (R^2,R^3) to an incipient double bond in the transition state appears to be the rate controlling factor.

In the absence of such stabilisation oxiranes formation may very easily by the normal course of events as is observed in the case of methylides[92].

Non stabilized π-sulfuranes eg.methylenedimethyl-sulfurane (82) when reacted with carbonyl compounds (83) such as benzaldehyde cyclohexanone and benzophenones afforded the epoxides (84) in fair to good yields (Scheme I.28). In the year 1961, Franzen et al[56] further extended the reaction of these ylides with α, β -unsaturated ketones and have shown that the exclusive formation of epoxides and non isolability of cyclopropanes. In the subsequent years Jhonson et al[60,93] took the credit of synthesizing substituted benzyldine phenyl sulfuranes (85) and have studied their reaction with carbonyl compounds (80) which lead to the formation of epoxides (87) exclusively (Scheme I.29). These study revealed that in π-sulfuranes unlike arsonium ylides[94], the course of the reaction with carbonyl compounds can not be attended by the nature of group present on the benzyllic position of the ylide carbanion, as a result these ylides[95] have been successfully employed for the synthesis of nitro substituted stibenes oxides which are quite inaccessible by their arsonium counterparts owing to the fact that nitro group favours the reaction to proceed in the direction of olefins formation.

Unlike non stabilized π-sulfuranes which are quite reactive against carbonyl function giving epoxides exclusively. Stabilized sulfuranes[62] do not react with carbonyl functions. Non reactivity towards carbonyl function is due to the decrease in nucleophilicity of these ylides. However Jhonson and Lacount[29]

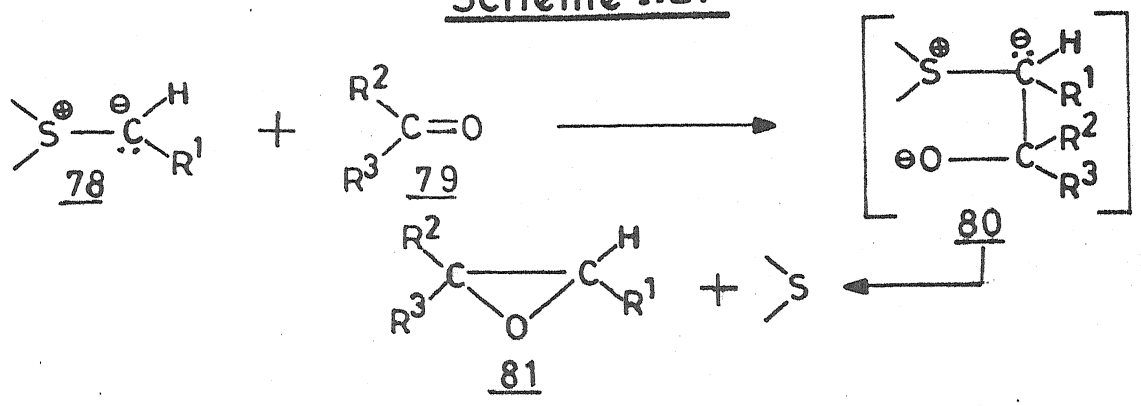
were first to study the reaction between stabilized π-sulfuranes fluorenylidene dimethyl sulfurane (88) and benzaldehyde (89), when epoxides (90) was found to be the exclusive product (Scheme I.30). Thereafter Payme et al[96] have demonstrated that stabilized ylides could be made to react with such systems in which carbonyl group is in conjugation with the highly electropositive group which enhances the electrophillic charecters of carbonyl atom, thus making them to enter into reaction with the sulfonium ylides.

2.10.2. With C=C double bonds(Synthesis of cyclopropane):

Prompted by the ability of π-sulfuranes to act as a versatile methylene transfer reagent as evidenced by the fact they form epoxides on their attack on carbonyl function, curiously aroused among the organic chemists to explore the reactivity of sulfuranes towards C=C. One of the first attempts in this direction came in the form of investigation carried out by Corey and Chaykovsky[30-33] which involved the nucleophillic addition of dimethyl oxosulfonium methylide (91) with chalcone (92) to produce trans-1-benzoyl-2-phenyl cyclopropane (93) (Scheme I.31).

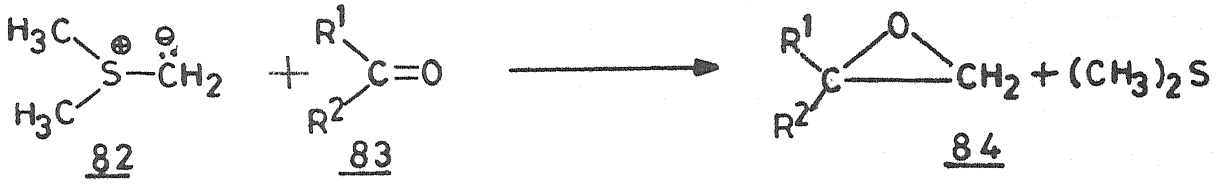
However cyclopropanation reactions starting from sulfonium salts (94) to form 1,2,3-tribenzoyl cyclopropane(97) were also known earlier[97] although the reaction mechanism of the reaction was not clear. Only in 1966 it was demonstrated[82-83]

Scheme I.27



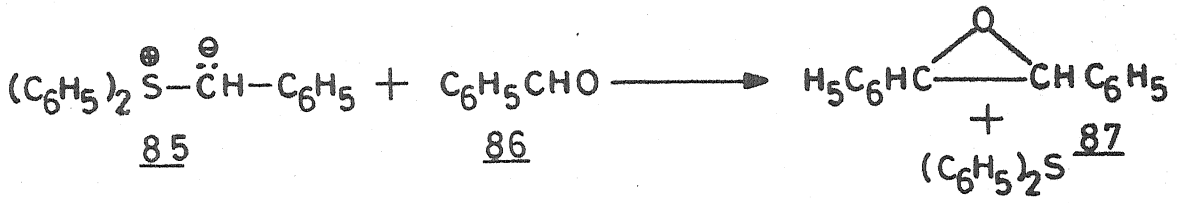
78 79 80 81

Scheme I.28



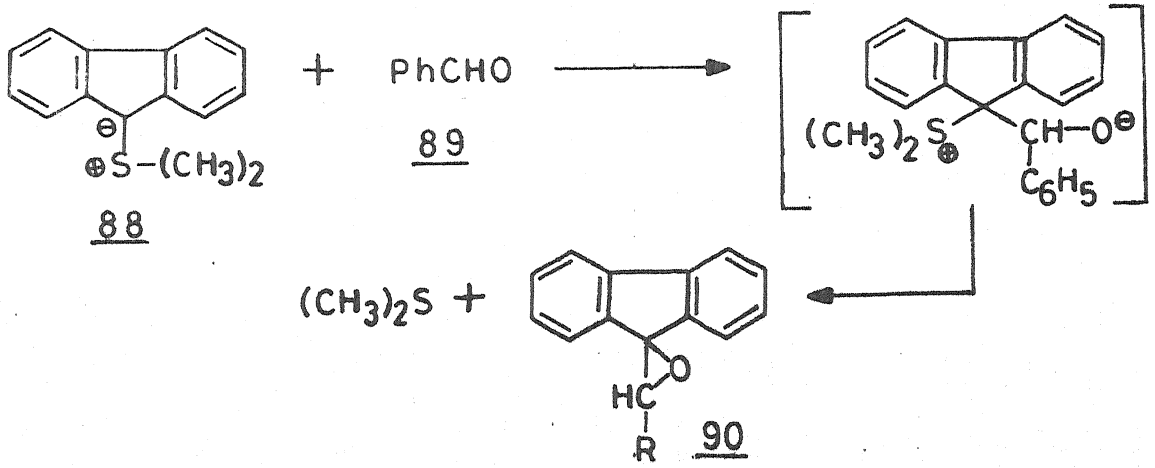
82 83 84

Scheme I.29



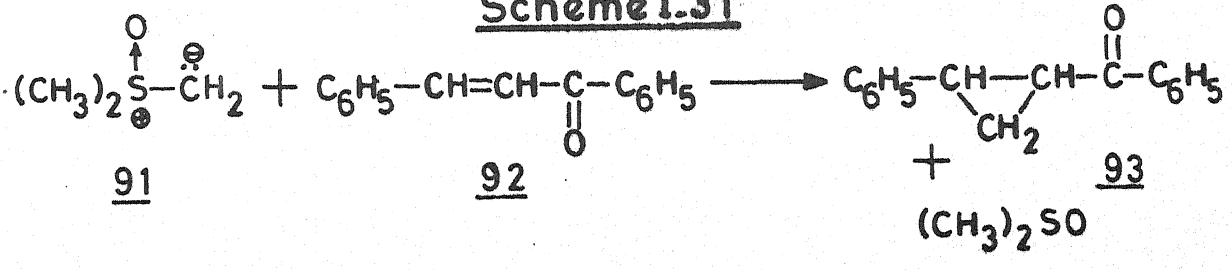
85 86 87

Scheme I.30



88 89 90

Scheme I.31



91 92 93

that the reaction proceeded by the addition of dimethylsulfonium phenacylidene (95) to dibenzoyl ethylene (96) (Scheme I.32). However the case with which cyclopropanation takes place depends on the nucleophi lic character of the ylide carbanion. This can be illustrated by the fact that non-stabilized π-sulfuranes readily attack over C=C bond, due to enhanced nucleophi licity by the absence of stabilization factors giving cyclopropane derivatives. On the otherhand, it was observed that stabilized sulfuranes which are relatively less nucleophil ic attack on conjugated C=C system only.

Subsequent to these investigations the method introducing cyclopropanes has become one of the most important in daily methods besides one involving carbene addition. Payme[98] has shown by studying the addition of carbethoxy dimethyl π-sulfuranes (98) to the hexanone (99) that the nucleophi lic methylene transfer takes place at the double bond to form cyclopropane (100) and not on carbonyl group (Scheme I.33). In this way cyclopropanated steroids[99] and nucleosides[100-101] have been synthesised.

2.10.3. With C-N double bond (Synthesis of Aziridines):

Franzen[32] and Corey[33] have studied the reaction of non stabilized π-sulfuranes methylene dimethyl sulfurane (101), with Schiff's bases (102), leading to the formation of a variety of aziridines (103) (Scheme I.34). Hoffman[102] et al have

demonstrated that the same ylide (101) can also affect other C-N double bond systems when he synthesised 1-azabicyclobutanes (105) by the direct condensation of the ylide (101) with aziridines (104)(Scheme I.35).

However the stabilized sulfonium ylides differ from the non stabilized sulfonium ylides in so far as their course of reaction with Schiff's bases is concerned and it was observed[103] that ylides (106) produce aryl amino cinnamates (108) and not aziridines (Scheme I.36).

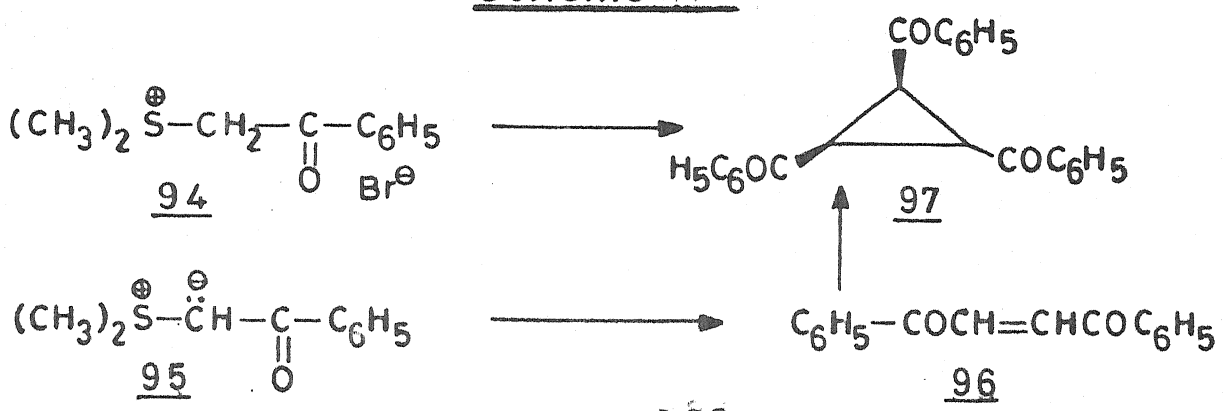
2.10.4. With C-S double bonds(Synthesis of Thioxirane):

Corey and Chaykovsky[33] have reported that methylene dimethyl sulfurane (109) on its reaction with benzothiophenone (110) affects the methylene transfer at C=S bond affording the thiooxirane (111). The reaction follows the same course as with benzophenone (Scheme I.37).

2.10.5. With N-O double bond :

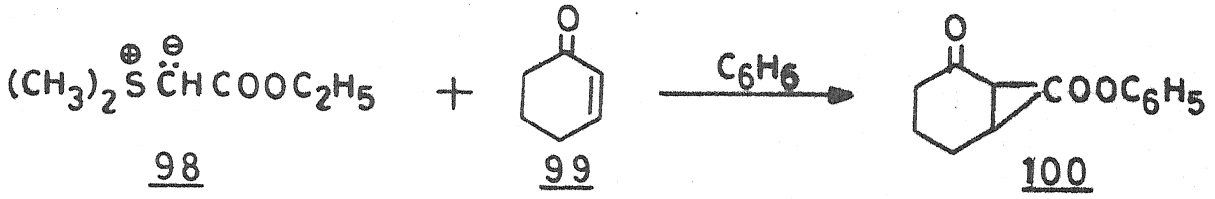
The reaction of nitro compound with sulfonium ylides leads to the synthesis of C-N double bond. Jhonson[54] demonstrated that it was fairly on addition, elimination methylene transfer reaction of sulfuranes which produces oxime. Thus fluoranylidene, dimethyl sulfurane (112) and nitrosobenzene (113) were shown to undergo an exothermic and rapid reaction to afford the nitrone-N-phenyl fluorenone ketoxime (114) (Scheme I.38).

Scheme I.32



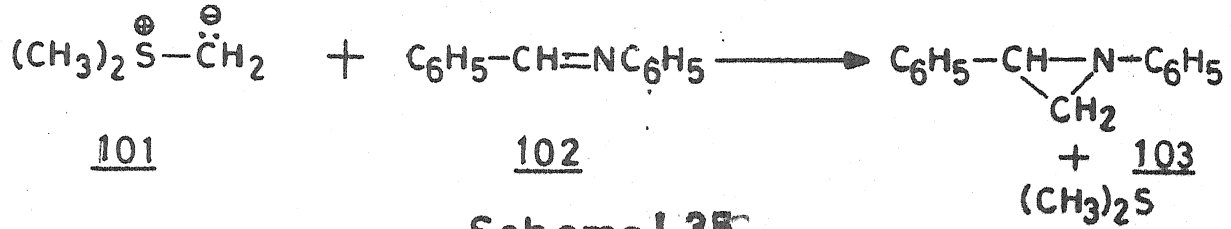
94 95 96 97

Scheme I.33



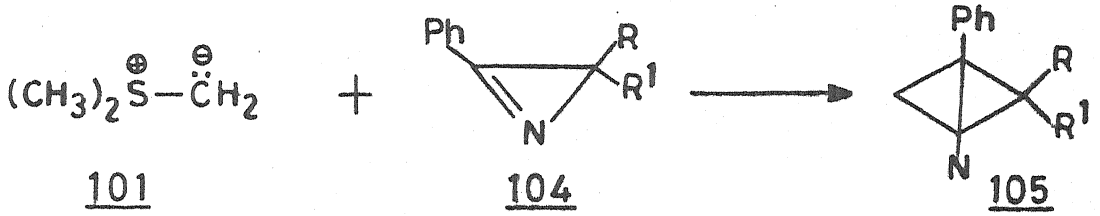
98 99 100

Scheme I.34



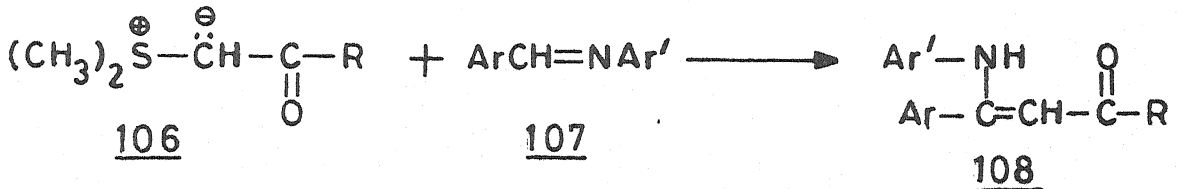
101 102 103

Scheme I.35



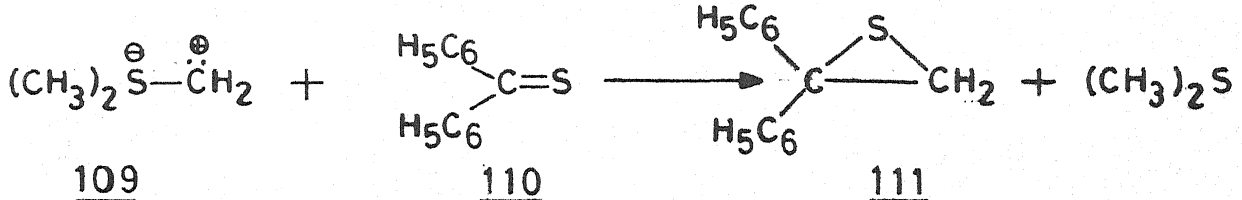
101 104 105

Scheme I.36



106 107 108

Scheme I.37



109 110 111

I.2.11. Metalation of π-sulfuranes :

The metalation reaction of π sulfuranes could not be explored until recently only preliminary studies on the reactions of inorganic compounds with the yields are reported[36].

However it has been shown that the sulfonium ylides (115) being co-ordinatively unsaturated, 1,2 dipolar complex of carbon serve as a good ligand for transitional metals(116) in various oxidation states and yields the markedly stable metal complexes (117) of sulfonium ylides(115) (Scheme I.39).

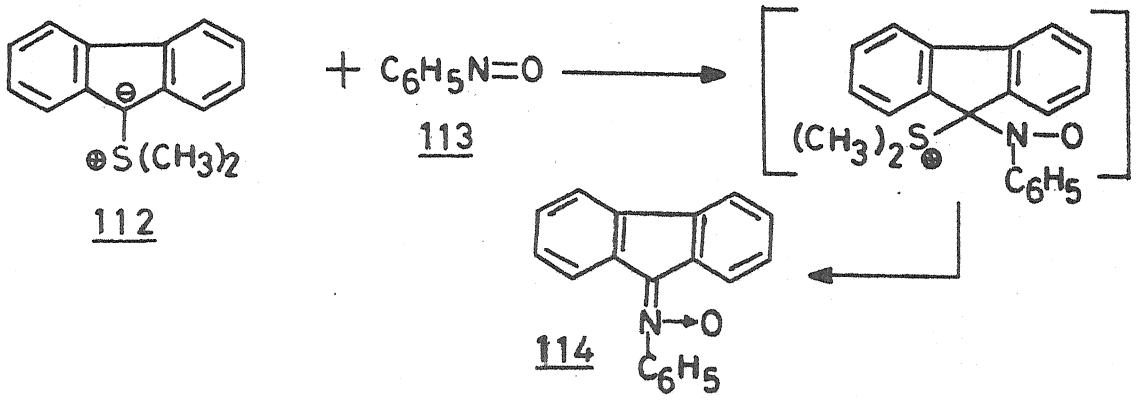
I.2.12. Elimination :

Evidence for the ∝-elimination is meagre[104]. However dimethyl sulfonium phenacylide (118) has been reported to add an cyclohexene (119) in the presence of cupric sulphate through ∝-elimination, giving cyclopropane (120)[105] other claims of ∝-elimination remain even more speculative.

I.2.13. Rearrangement :

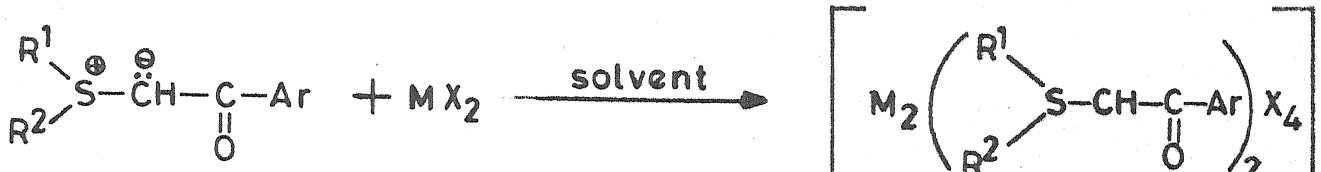
As revealed by the literature π-sulfuranes have been involved in several types of rearrangements. Thomson and Stevans[106] have reported that benzylmethylphenacyl sulfonium bromide (121) undergo of phenacylidene benzyl methyl sulfurane (122) to yields the rearrangement product (123)(Scheme I.41). Houser et al[107] have demonstrated that the benzyl dimethyl

Scheme I.38



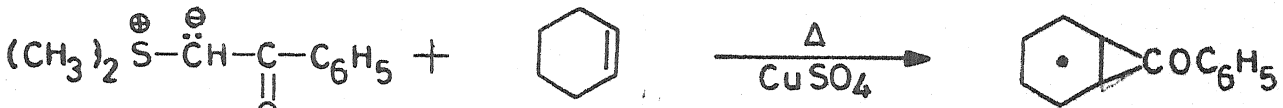
112 113 114

Scheme I.39



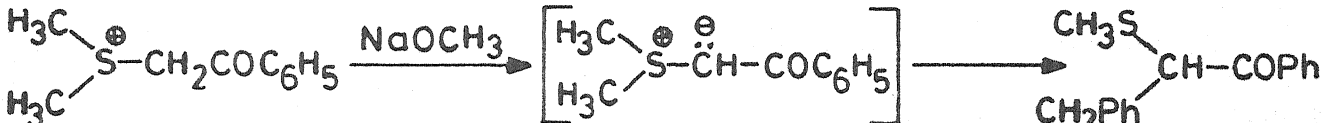
115 116 117

Scheme I.40



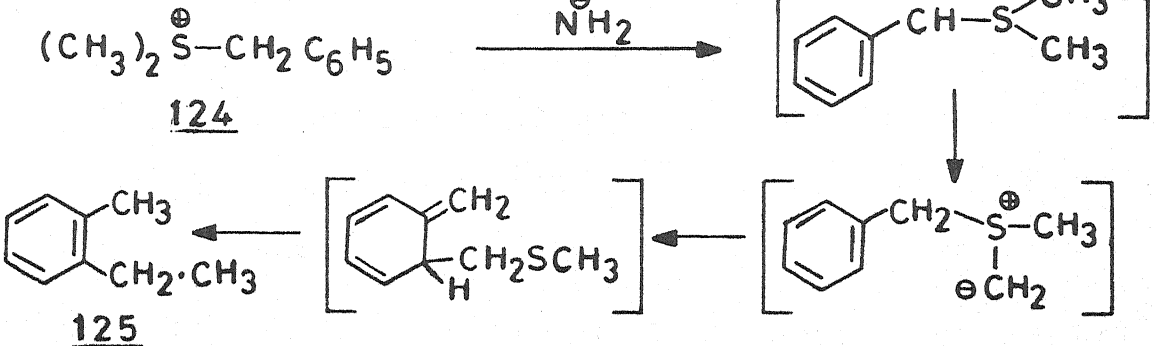
118 119 120

Scheme I.41



121 122 123

Scheme I.42



124 125

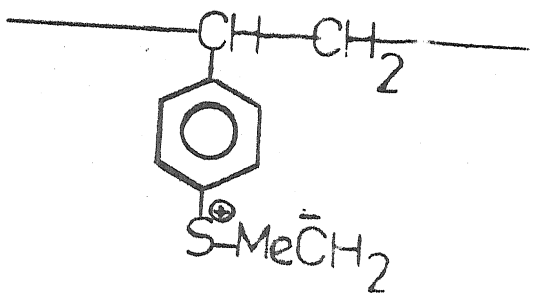
sulfonium ion (124) in the presence of amide ion, undergoes Sommetal rearrangement to afford O-methyl benzyl methyl sulfide (125) (Scheme I.42).

In recent years, these rearrangements have been produced to be great synthetic importance particularily in the synthesis of natural products[72,108].

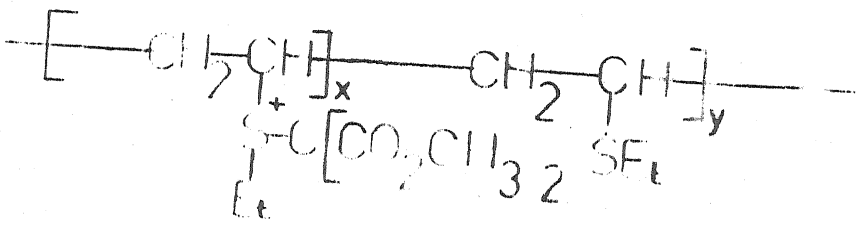
I.2.14. π-Sulfuranes in the prepration of polymers :

In an attempt to prepare sulfonium ylide polymer viz. sulfurane polymer Tanimoto and et al[109,110] comming out the reaction of sulfonium salt with benzaldehyde in presence of base and obtained styrene oxide. The reaction was carried out to proceed via ylide polymer formation (126) which was unstable and has not been isolated.

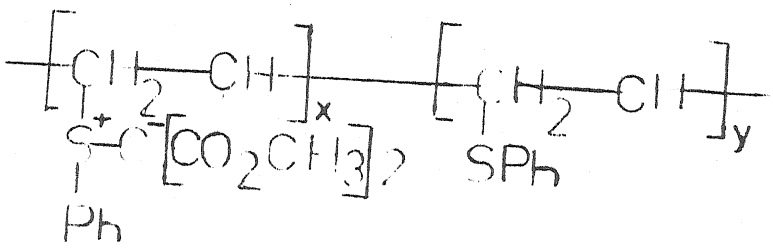
Later on Kondo et al[111] and his collegues reported on the synthesis of poly (vinyl sulfonium ylide) with a trivalent sulfur attached directly to the polymer chain, Poly [ethyl vinyl sulfonium bis (methoxy carbonyl) methylide] (127) was prepared by irradiation of a benzene solution of poly (ethyl vinyl sulfide) and dimethyl diazomelonate in a pyrex tube by a high pressure mercury lamp. In the similar manner, an attempt was made to prepare poly [Phenyl vinyl sulfonium bis(methoxy carbonyl) methylide] (128), but it was not successful. However, this compound was obtained by the thermal reaction of



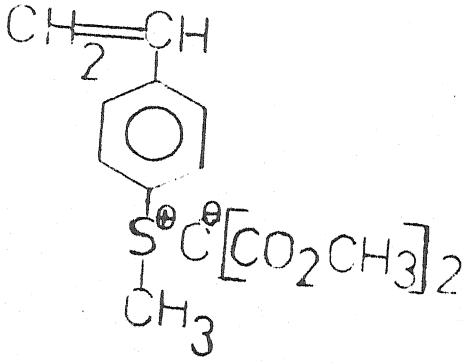
(126)



(127)



(128)



(129)

diazomalonate and poly (phenyl vinyl sulfide) in the presence of cupric sulphate as catalyst in benzene.

The structure of these ylide polymers were determined and confirmed by IR and NMR spectra. These were the first stable sulfonium ylide polymers reported in the literature. They are very important for such industrial uses as ion exchange resins, polymer supports, peptide synthesis, polymeric reagents and polyelectrolytes. Also in 1977, Hass Mereau[112] found that when poly (4-vinyl pyridine) was quaternized with bromomalonamide, two polymeric quaternary salts resulted. These polyelectrolyte products were subjected to thermal decyanation at 7200°C to give isocyanic acid or its isomer cyanic acid. The addition of base to the solution of electrolyte in water gave a yellow polymeric ylide.

In a pioneering article, Farrall et al[113] reported the preparation of fully regenerable sulfonium salts anchored to an insoluble polymer and their ylides with carbonyl compounds. Their results clearly indicate that phase transfer catalysis is the method of choice for the generation of sulfonium ylides on insoluble resins from a polymeric sulfonium salt.

Kondo maintained his interest in this area and with his collaborators[111] he made detained investigation on the polymerisation and prepration of methyl-4-vinyl phenyl-sulfonium bis(methoxy carbonyl) methylide (129) as a new kind of stable

vinyl monomer containing the sulfonium ylide structure. It was prepared by heating a solution of 4-methyl thiostyrene, dimethyldiazomalonate, and t-butyl catechol in chlorobenzene at 90°C for 10 hours in the presence of anhydride cupric sulphate and (129) was polymerized by using $\alpha - \alpha'$ axobisiso-butyronitrile (AIBN) as initiator and dimethylsulfoxide as solvent at 60°C. The structure of polymer was confirmed by IR and NMR spectra and elemental analysis. In addition, this monomeric ylide was copoly-merised with vinyl monomers such as methyl methacrylate (MMA) and styrene.

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CHAPTER II

CHAPTER-II

SYNTHESIS OF 1,3,5-TRISUBSTITUTED NAPHTHALENES USING NON STABILIZED ω-SULFURANES : REACTION OF O-SUBSTITUTED BENZYL DIMETHYL SULFONIUM BROMIDES WITH α, β -UNSATURATED KETONES.

II.1. ABSTRACT :

O-chlorobenzyldimethylsulfonium bromide, O-bromobenzyl-dimethyl sulfonium bromide and O-nitrobenzyldimethyl sulfonium bromide have been prepared by the reaction of O-chlorobenzyl bromide, O-bromobenzyl bromide and O-nitrobenzyl bromide with dimethyl sulfide in benzene in an atmosphere of nitrogen at reflux temperature in fair to good yields. These sulfonium, salts on reaction with base generated corresponding O-substituted benzylidenedimethyl sulfuranes in situ. The reaction of these salts or sulfuranes with a wide range of substituted benzylidene-acetophenones in presence of anhydrous aluminium chloride or zinc chloride in the mixture of ammonium acetate and acetic acid gave 1,3,5-triarylnaphthalenes in good yields. Aluminium chloride or zinc chloride in acetic acid is used as cyclization agent. The structures of naphthalene derivatives were confirmed by elemental analysis, IR and NMR spectral data.

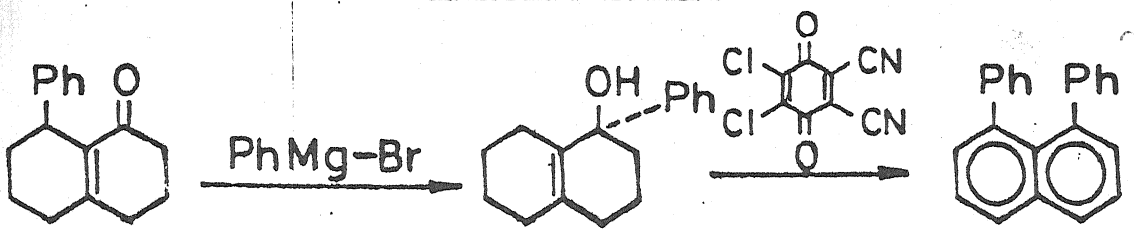
II.2. INTRODUCTION :

The various methods reported for the synthesis involved several steps and the yields of the final product was also poor. The house et al[1-2] were the first who attempted to prepare

naphthalene derivatives by the reaction of 8,phenyl Δ^{1-10}-octal-1-one (1) with phenyl magnesium bromide to form an alcohal (2), which underwent dehydrogenation and dehydration with 2,3-dichloro-5,6-dicynobenzoquinone in boiling benzene to afford to give desired product (3)(Scheme II.1). Since the route involved harsh reaction conditions and yields of the final product was also very poor. Bailey et al[3] reported another route which involved several steps for the synthesis of 1,8-dimethyl naphthalene (9) according to this synthesis first the reduction of 1,4,5,8,9,10-hexahydro-1,4-dioxo-5-phenylnaphthalene (4) took place. The resulting product (5) thioketals (6) with ethanol thio desulphurization with Raney nickel and the subsequent treatment of the resulting product (7) with phenyl lithium to give 1-transhydroxy -cis-syn-1,8-diphenyl decaline (8) were carried out. The product (8) on dehydrogenation with Pd/C carbon gave 1,8-diphenyl naphthalene (9)(Scheme II.2).

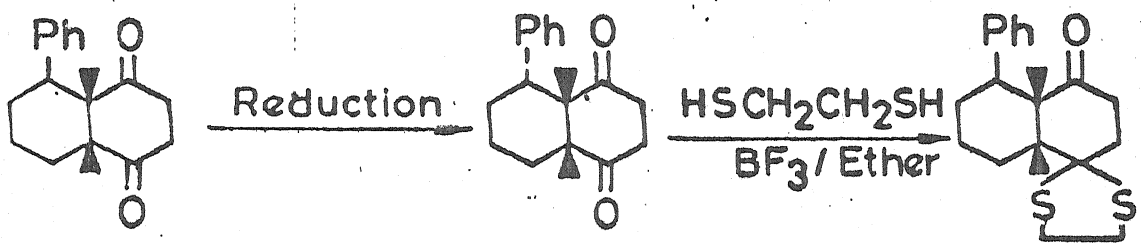
Later on a convinient and facile route was reported by Krohnke's et al[4] for the synthesis of diaryl naphthalene derivatives which involved the candensation of benzylpyridinium bromide (10) with benzal acetophenone (11). In presence of zinc chloride to give 1,3-diphenyl naphthalene (12)(Scheme II.3). This Krohnke's[4] method proved better than aforesaid mention methods because it involved single step and gave better yields of final product. Lateron Tewari et al[5] and Gupta et al[6] also duplicated the reaction and reported the detail experimental

Scheme II·1·

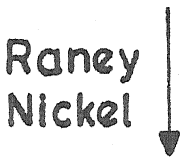


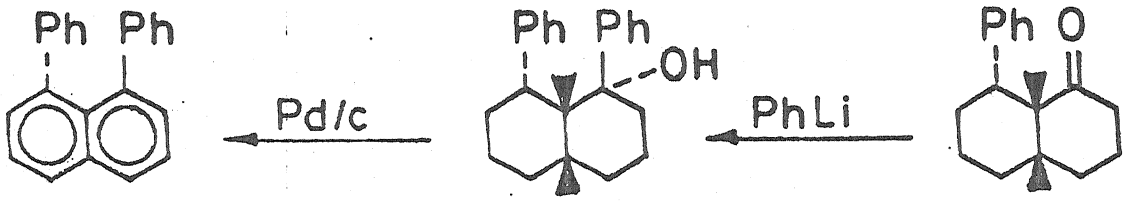
1 2 3

Scheme II·2



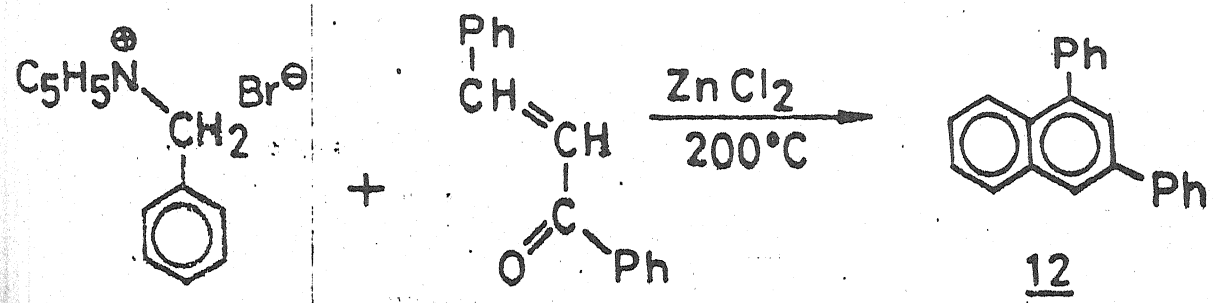
4 5 6





9 8 7

Scheme II·3



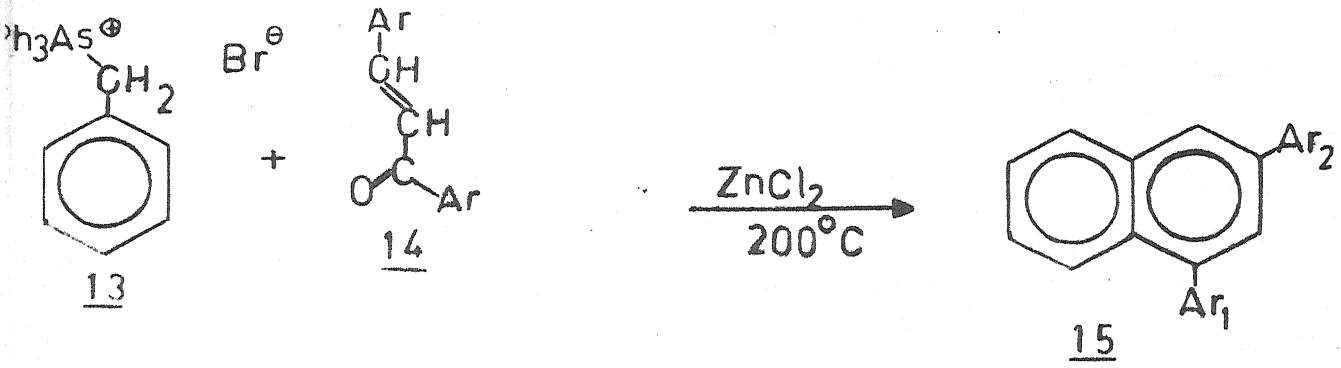
10 11 12

conditions for the prepration of 1,3-diaryl naphthalene. Further more, this reaction selective introduction of substituents at 1 and 5 positions of the naphthalene nucleous. However a few reactions following this procedure have been reported but detailed experimental conditions have not been described. Prompted from this work seemed to be of great interest to explore the domain of applicability of this new route.

Subsequently Gupta et al[7] have synthesized naphthalene nucleous (15) by the use of phenacyltriphenylarsonium salts (13) with α, β-unsaturated ketones (14) in presence of anhydrous zinc chloride in the mixture of sodium acetate and glacial acetic acid. The course of reaction of arsonium salts was also found to similar to that of corresponding pyridinium salts reported earlier 5,6 (Scheme II.4).

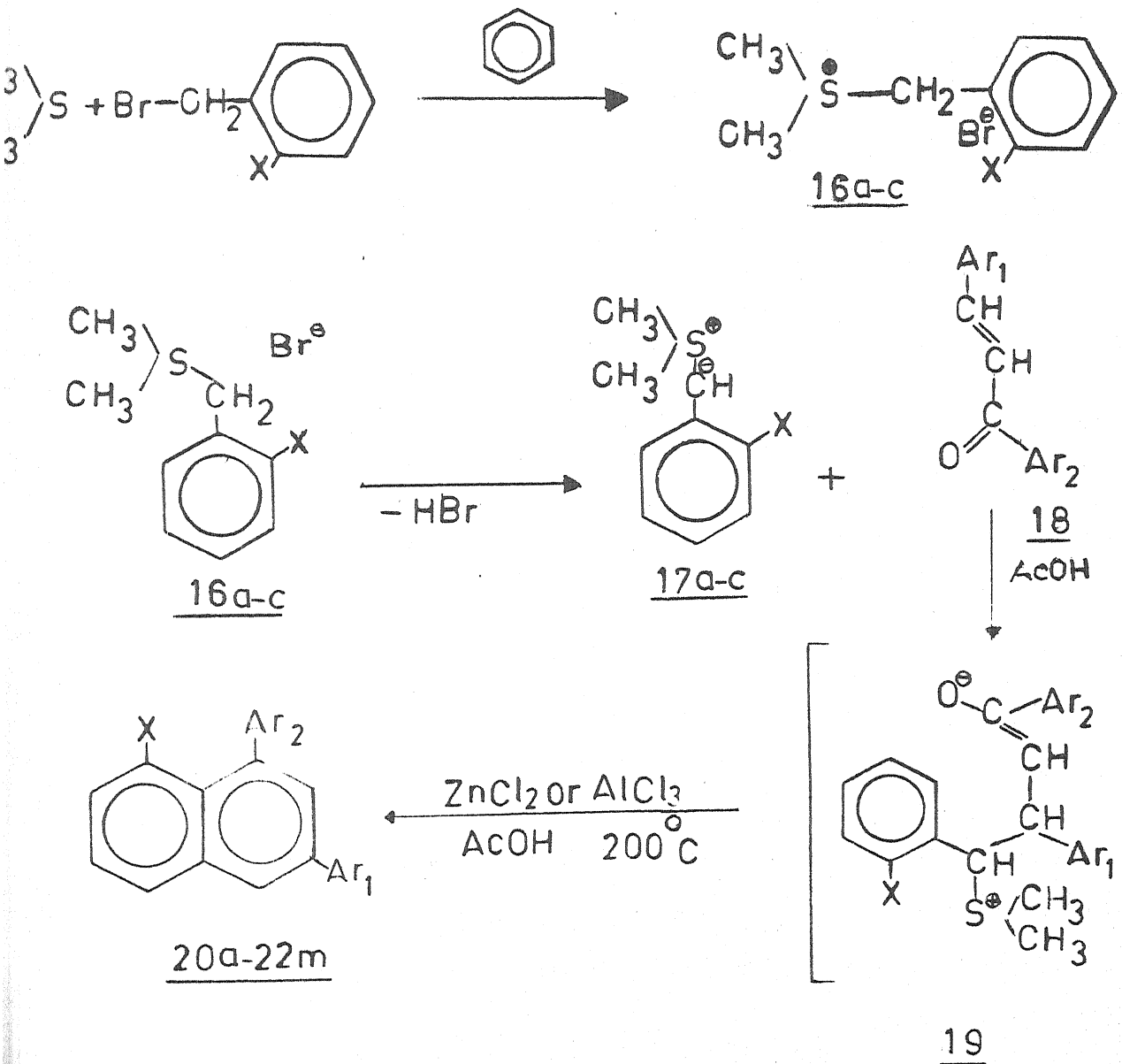
The pyridinium[6] and arsonium salts[7] were successfully utilized in the synthesis of naphthalene nucleous as reported earlier. It was therefore thought worthwhile to investigate an alternative route for the synthesis of naphthalene derivatives which the reaction of sulfonium salts with α, β-unsaturated ketones with view to compare the course of reaction of sulfonium salt and corresponding sulfonium ylides with these of analogous pyridinium and arsonium salts and corresponding ylides of V group elements.

Scheme II.4



13 14 15

Scheme II.5



16a-c 17a-c 18 19 20a-22m

II.3. RESULTS & DISCUSSION :

The reaction of O-chlorobenzyl bromide, O-bromobenzyl bromide and O-nitrobenzyl bromide with dimethyl sulphide in benzene at reflux temperature under nitrogen atmosphere gave O-chlorobenzyldimethyl sulfonium bromide (16a), O-bromobenzyl-dimethyl sulfonium bromide (16b) and O-nitrobenzyl dimethyl sulfonium bromide (16c) (Scheme II.5).

The structures of these sulfonium salts (16 a-c) were evidenced on the basis of IR and NMR data. The IR spectra of these salts showed charecterstic absorption bands of strong intensity at, 3045 Cm^{-1}, 3040 Cm^{-1} and 3000 Cm^{-1} and 3060 Cm^{-1} respectively due to C-H stretching vibration bands of methylene group attached to a position adjecent to S-atom. This diagnostic absorption band due to nitro group in the salt (16c) were obtained at 1520 Cm^{-1}, 1300 Cm^{-1}. The NMR spectra of (16 a-c) showed a strong singlet in the range δ 5.0-5.3 due to methylene group attached to the sulfonium group. A sharp singlet at δ3.0-3.2 were due to two methyl groups directly attached to sulfonium group and aromatic protons were observed in the range δ7.05-8.45.

The reaction of these salts (16 a-c) were carried out with a wide range of α,β-unsaturated carbonyl compounds in presence of anhydrous aluminium chloride or zinc chloride in a mixture of sodium acetate and acetic acid at 200°C to afford 1,3-diaryl-5-chloro naphthalenes (20 a-m), 1,3-diaryl-5-bromo

naphthalenes (21 a-m) and 1,3-diaryl-5-nitronaphthalenes (22a-m) in 50-75% yields. It was however, observed that the yields of resulting naphthalenes were dependent upon the nature of substituents attached to sulfonium salts (16a-c) as well as to the α- β-unsaturated ketones. The reactivity of salt(16c) was lower than salts (16a-b) because of -I effect of NO_2 which stabilized the carbanion formation. Hence, salt (16c) afforded lower yields of naphthalene derivatives than the salt (16a-b).

The reaction seems to proceed via the intermediates of a betaine type of derivatives (19), which is formed by the nucleophillic attack of the ylide carbons (17a-c) presumbly generated in situ by dehydrohalogenation of salts (16a-c), on the β carbon of α,β -unsaturated ketones (18), betaine (19), then undergoes cyclization in presence of anhydrous zinc chloride or aluminium chloride used as cyclization agent to afford naphthalene derivatives (20a-22m) obtained in the present investigation were crystalline solids usually soluble in chloroform, dimethyl sulfide and acetone. All physical data have been reported in table II.1. All the compounds are new and gave satisfactory elemental analysis. The IR spectral[8] data (table II.2) of naphthalene derivatives showed a double absorption maxima in the region 1630-1620 Cm^{-1} which were assigned to the stretching vibrations of carbon-carbon double bond. The strong bands in the region 900-850 Cm^{-1} were diagnostic absorption of polynuclear aromatics. The nitro group of the

products showed a strong symmetrical stretching band at 1350-1330 Cm^{-1}. The NMR spectra of compound in general, exhibited aromatic multiplet in the range δ 6.50-8.50 methyl protons at δ 2.25-2.30 and methoxy protons at δ 3.75-3.80.

II.4. EXPERIMENTAL :

II.4.1. General techniques :

Until and unless not specified, here and hereinafter melting points were recorded in degrees centigrade on a Gallen Kamp appratus and are uncorrected. IR spectra were recorded on a Perkin-Elmer infracord spectrophotometer using KBr phase. Varian A-60 and A-100 spectrometer was used to record NMR spectra using tetramethylsilane (TMS) as an internal standard. The products were separated and purified by column chromatography using neutral alumina as absorbent. Glass microscope slides coated with silica gel G were used for thin layer chromatography (TLC). The spots on slides were developed by placing them in iodine chamber.

II.4.2. Starting materials :

All the reagents were obtained from commercial sources i.e. B.D.H., S. Merck, E. Merck etc. The starting materials were prepared according to references cited. Thus O-chlorobenzyl bromide, O-bromobenzyl bromide and O-nitrobenzyl bromide were prepared by the direct bromination of corresponding O-substituted

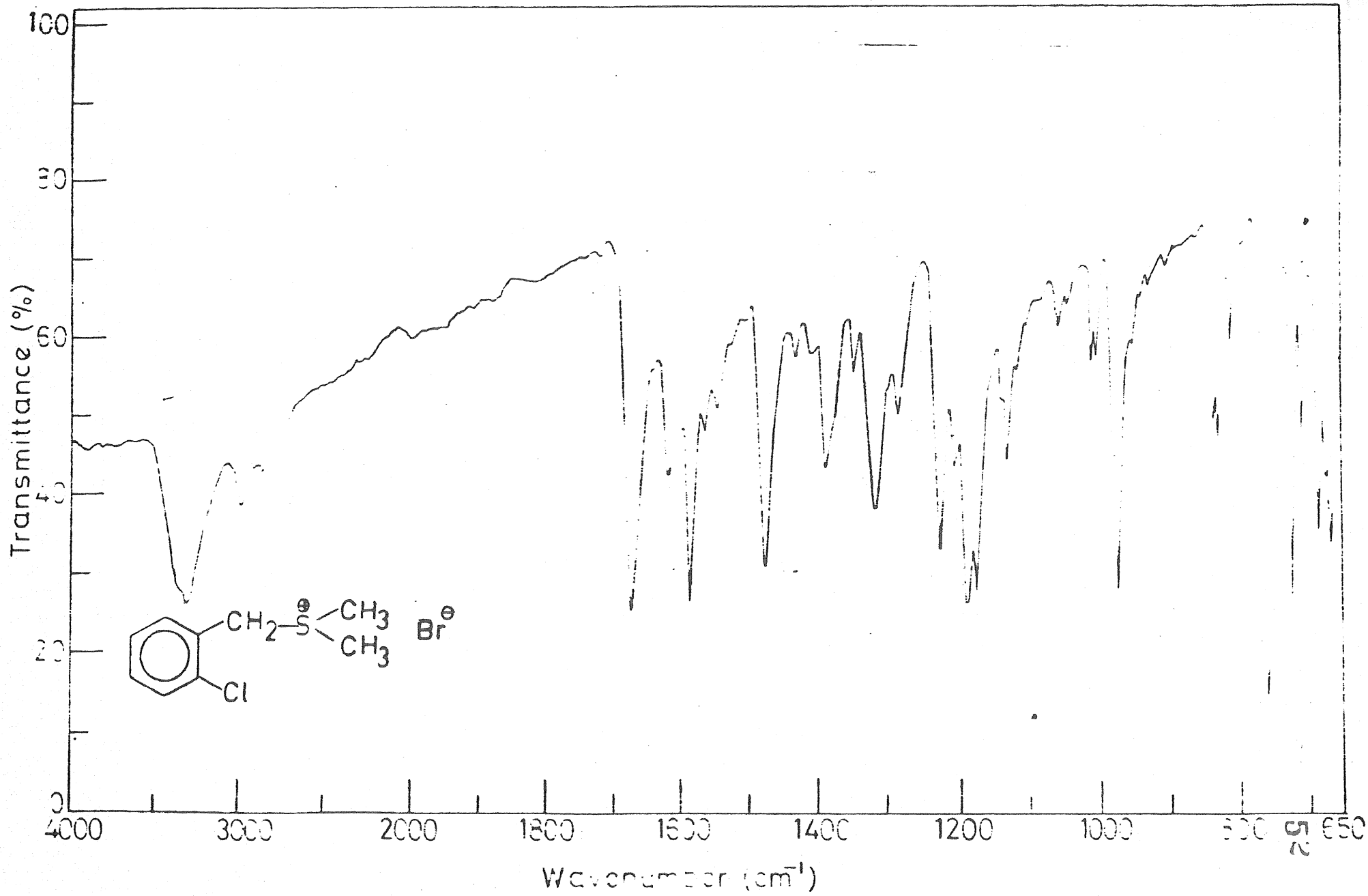


FIG. II.1 IR SPECTRUM OF 16a.

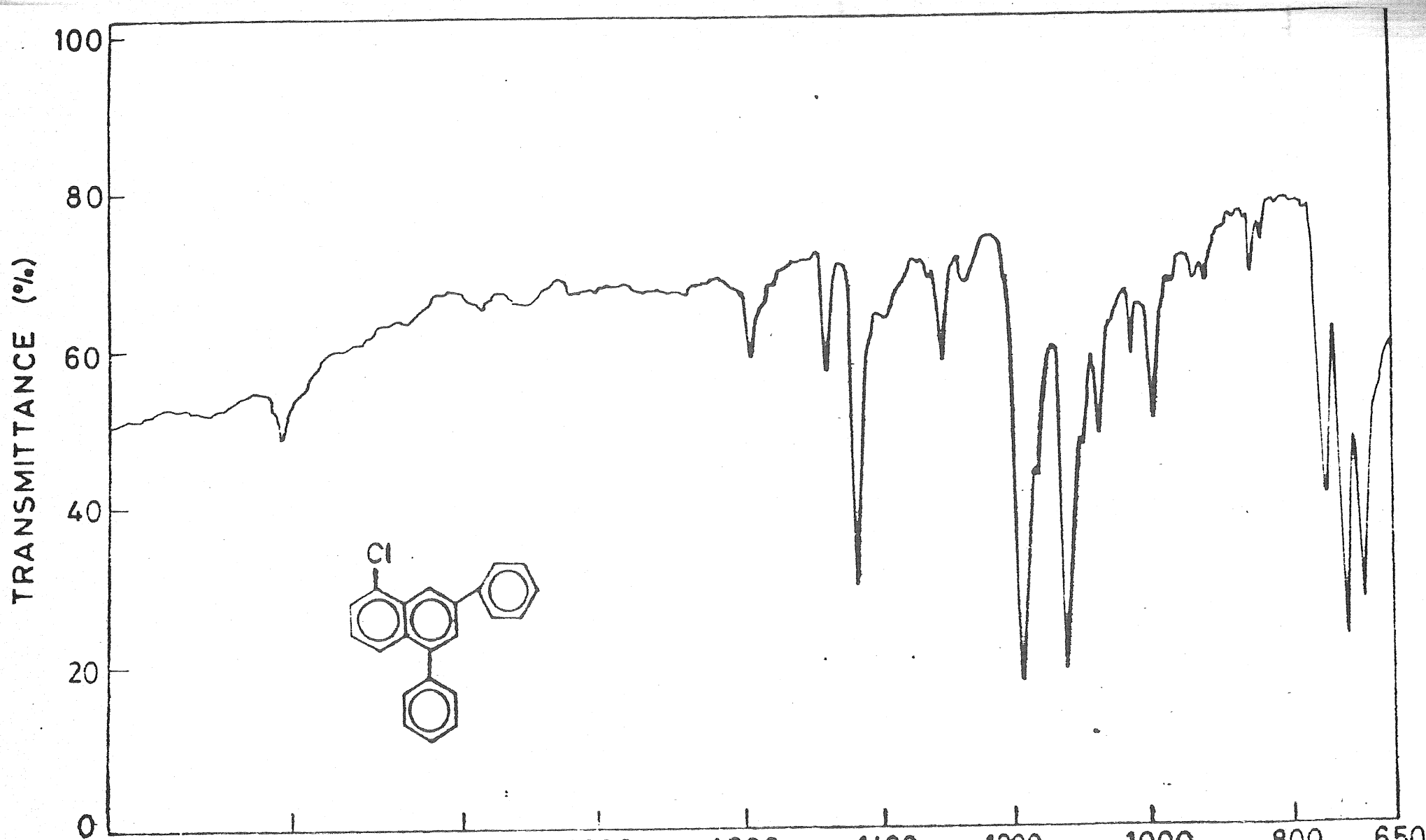


FIG. II·2 IR SPECTRUM OF COMPOUND (20a)

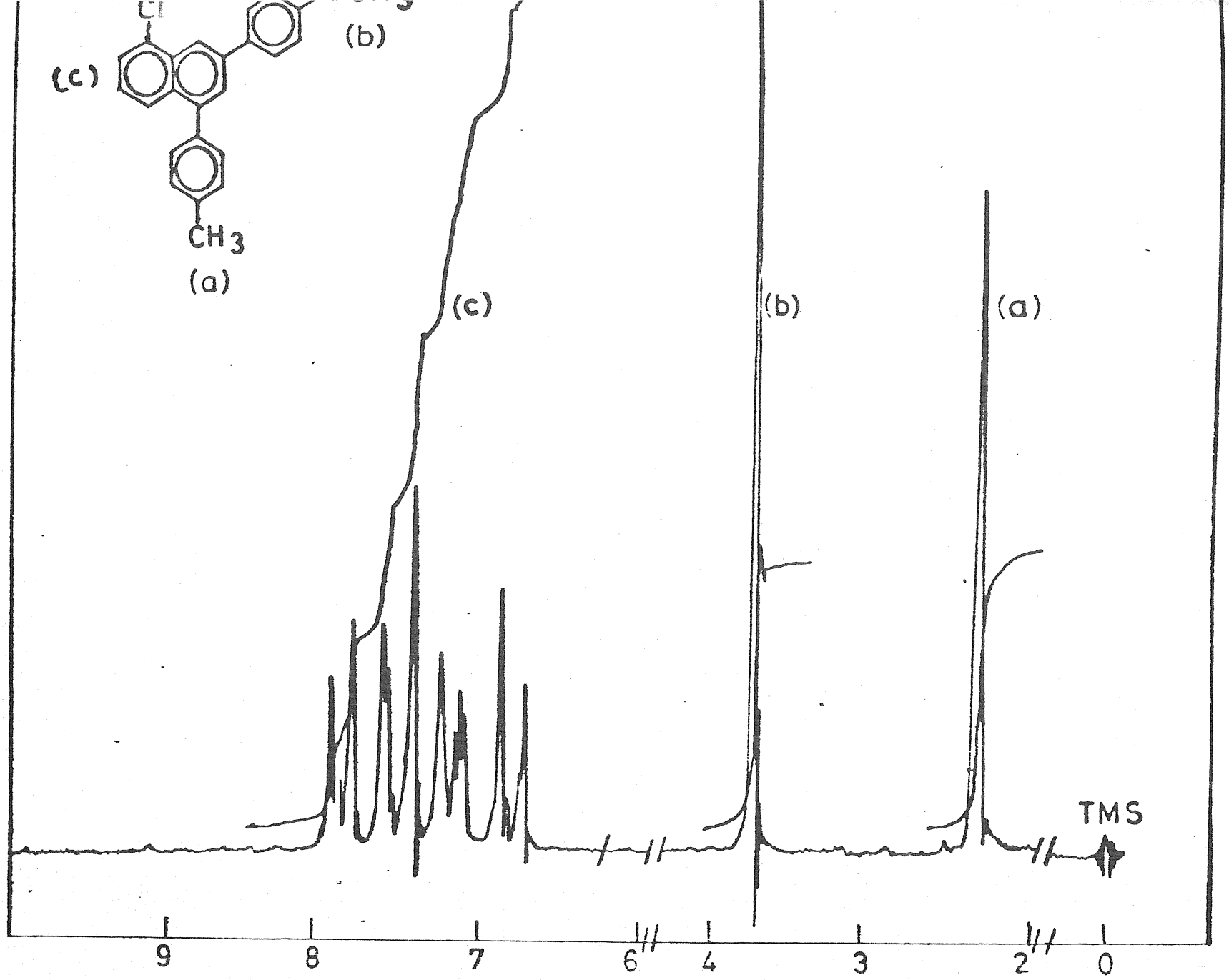


FIG. II · 3 NMR SPECTRUM OF COMPOUND (20g)

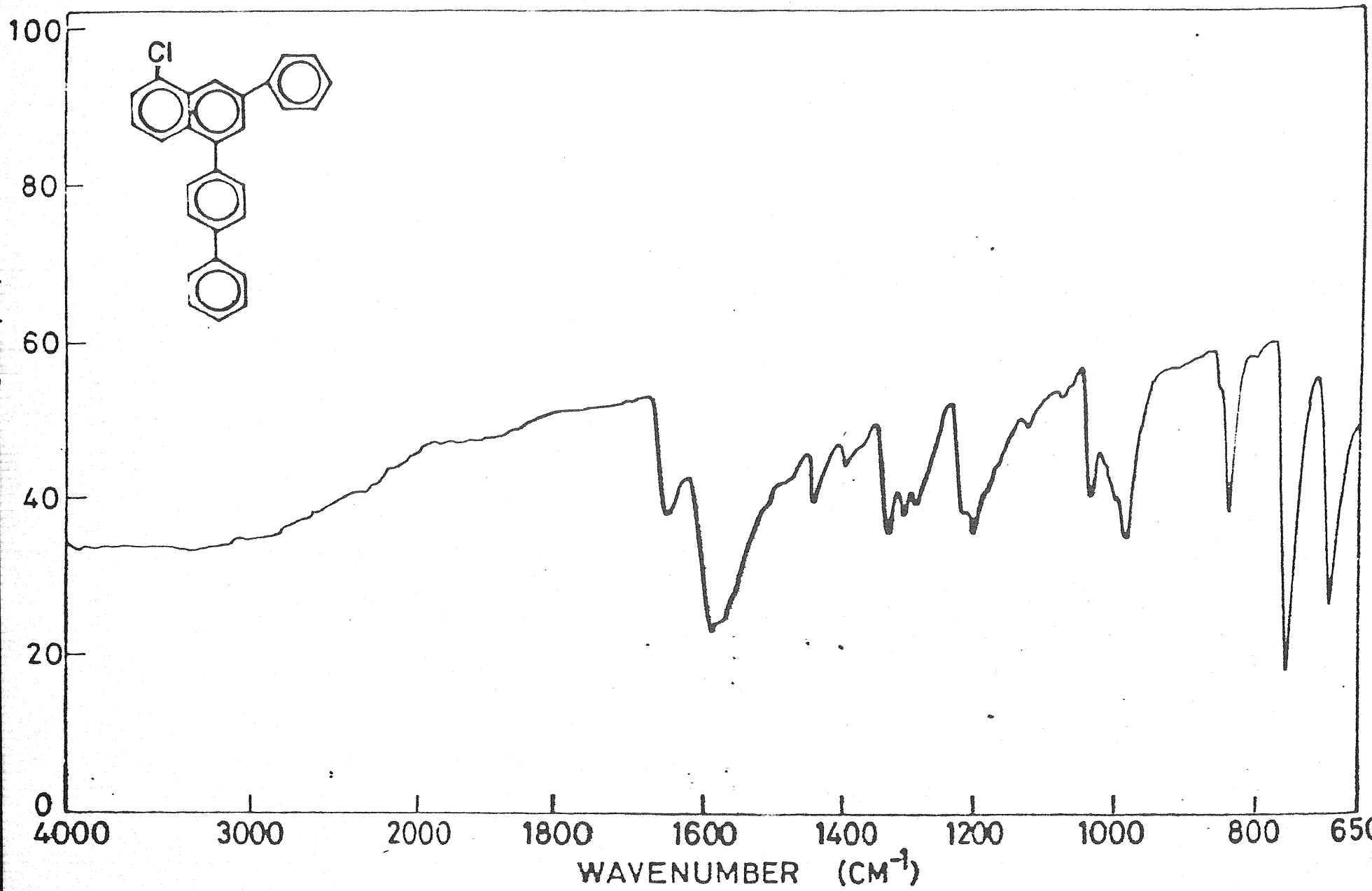


FIG II.4. IR SPECTRUM OF COMPOUND (201)

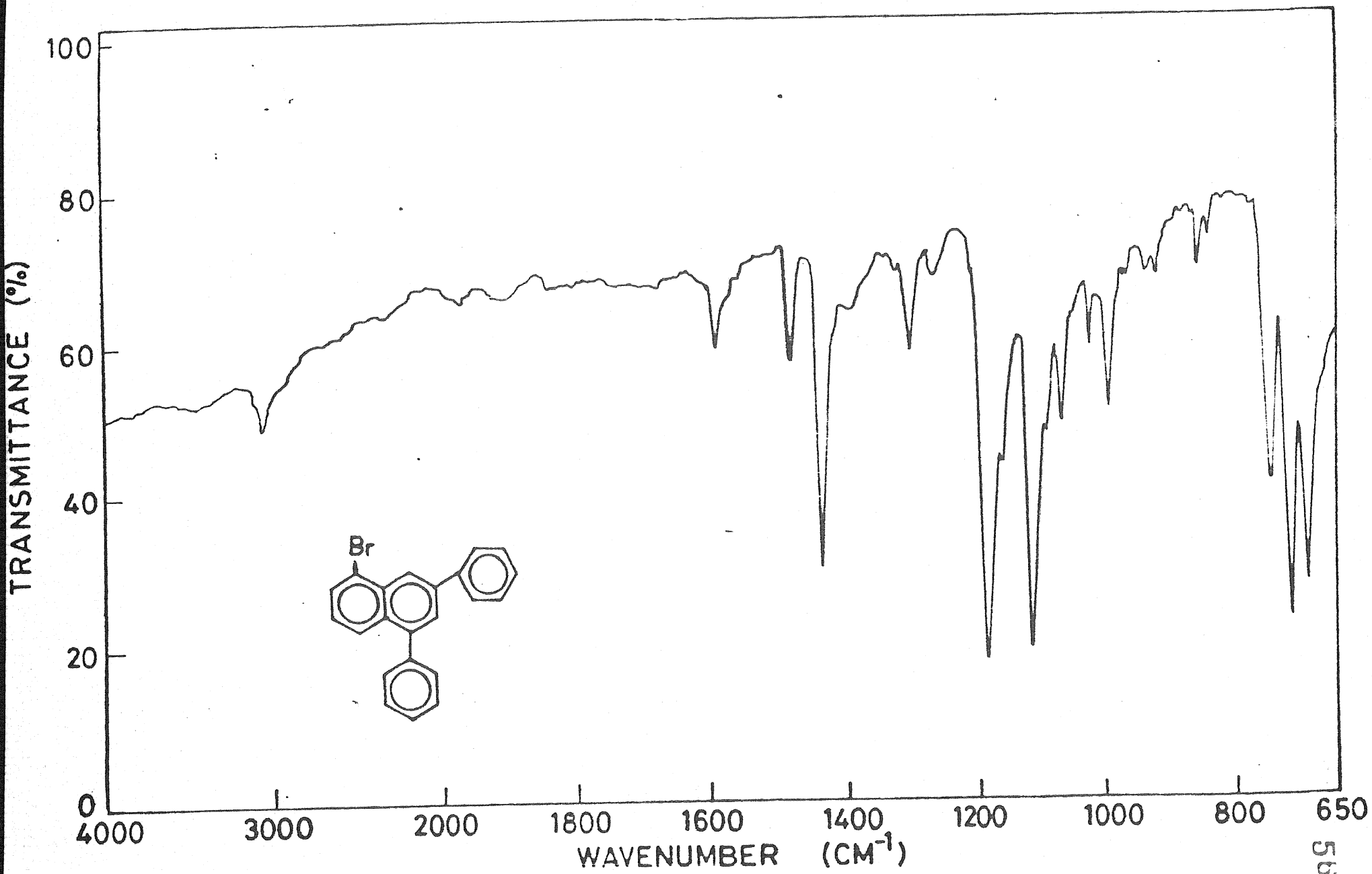


FIG. II ·5 IR SPECTRUM OF COMPOUND (2.1a)

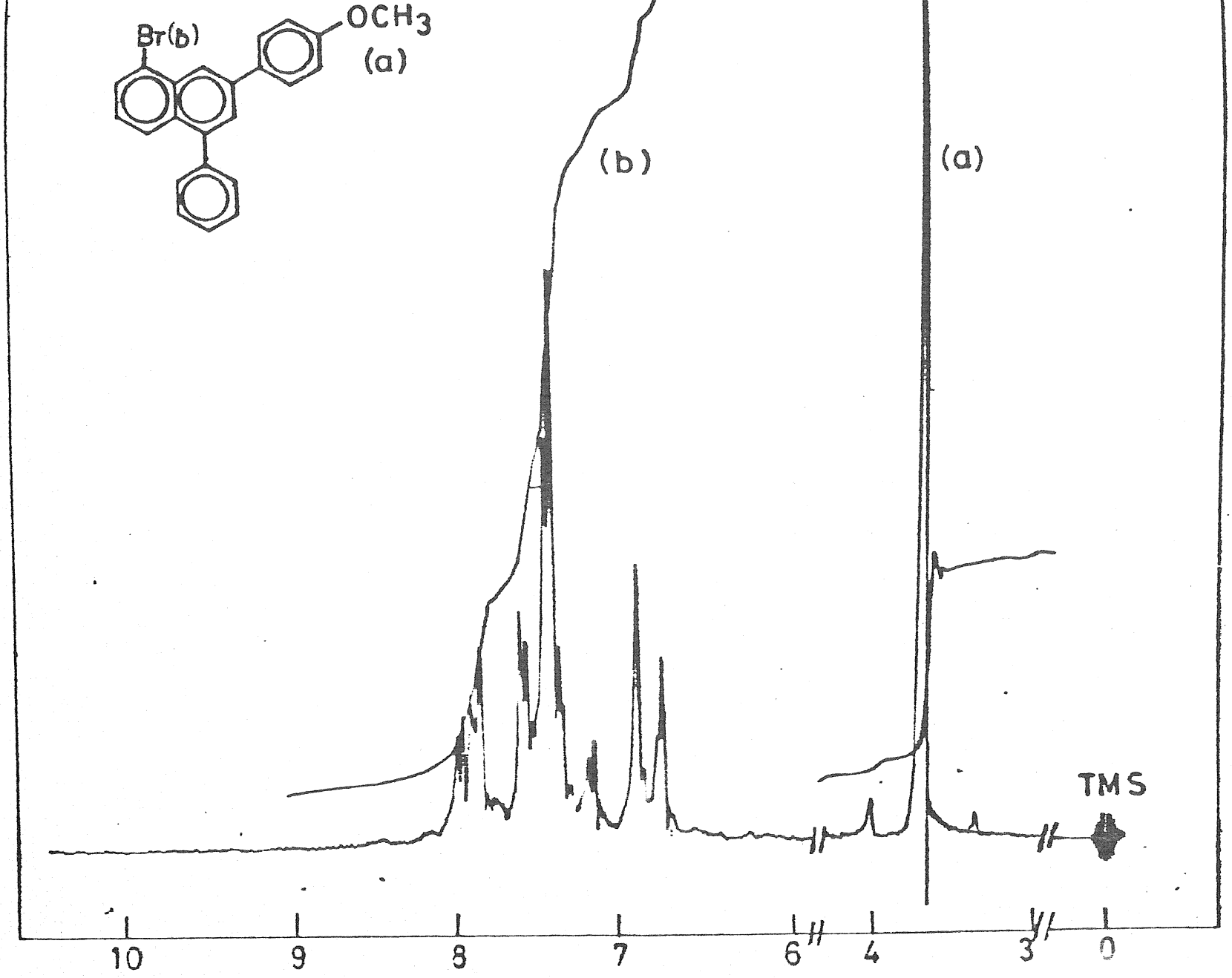


FIG.II.6 NMR SPECTRA OF COMPOUND (21c)

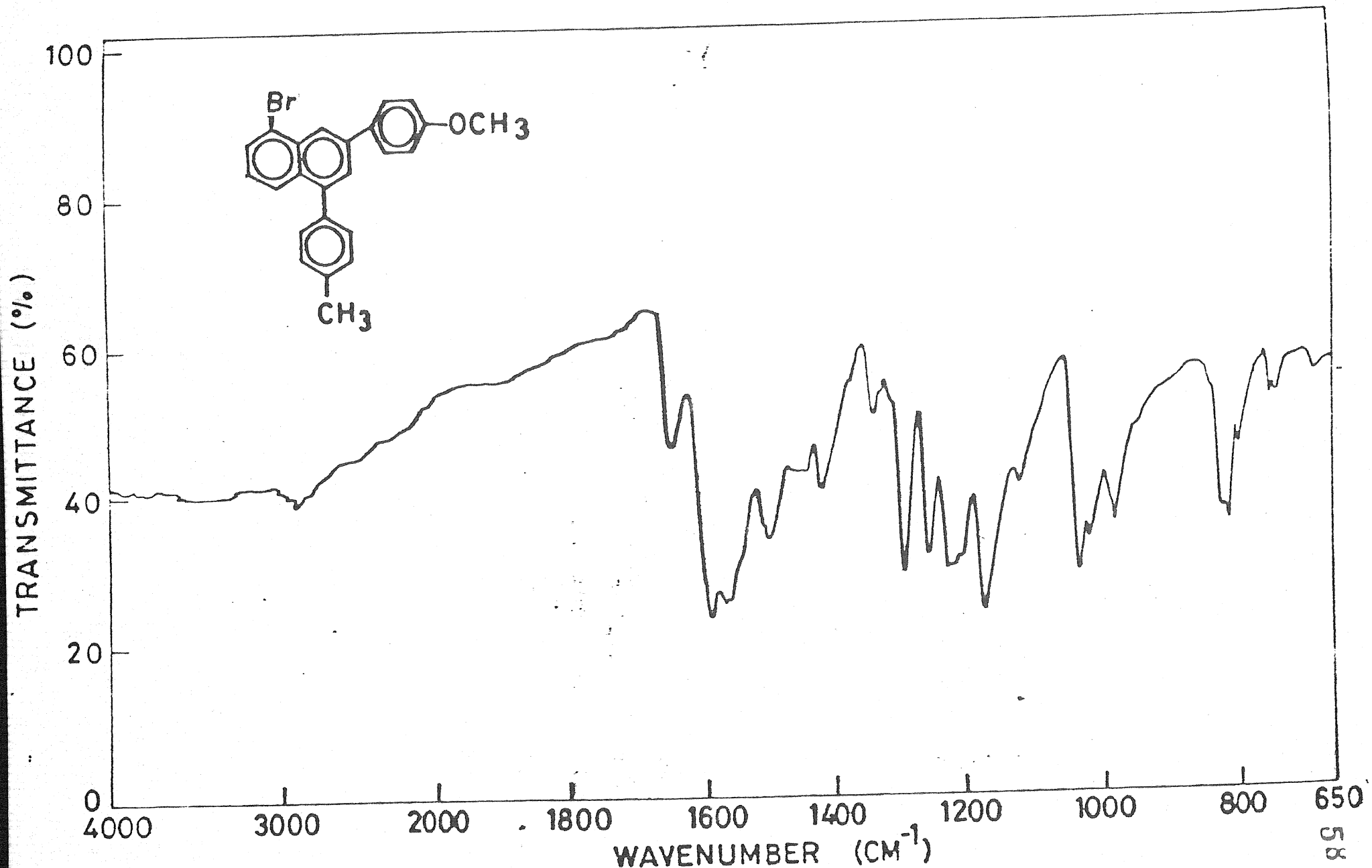


FIG II.7 IR SPECTRUM OF COMPOUND (219)

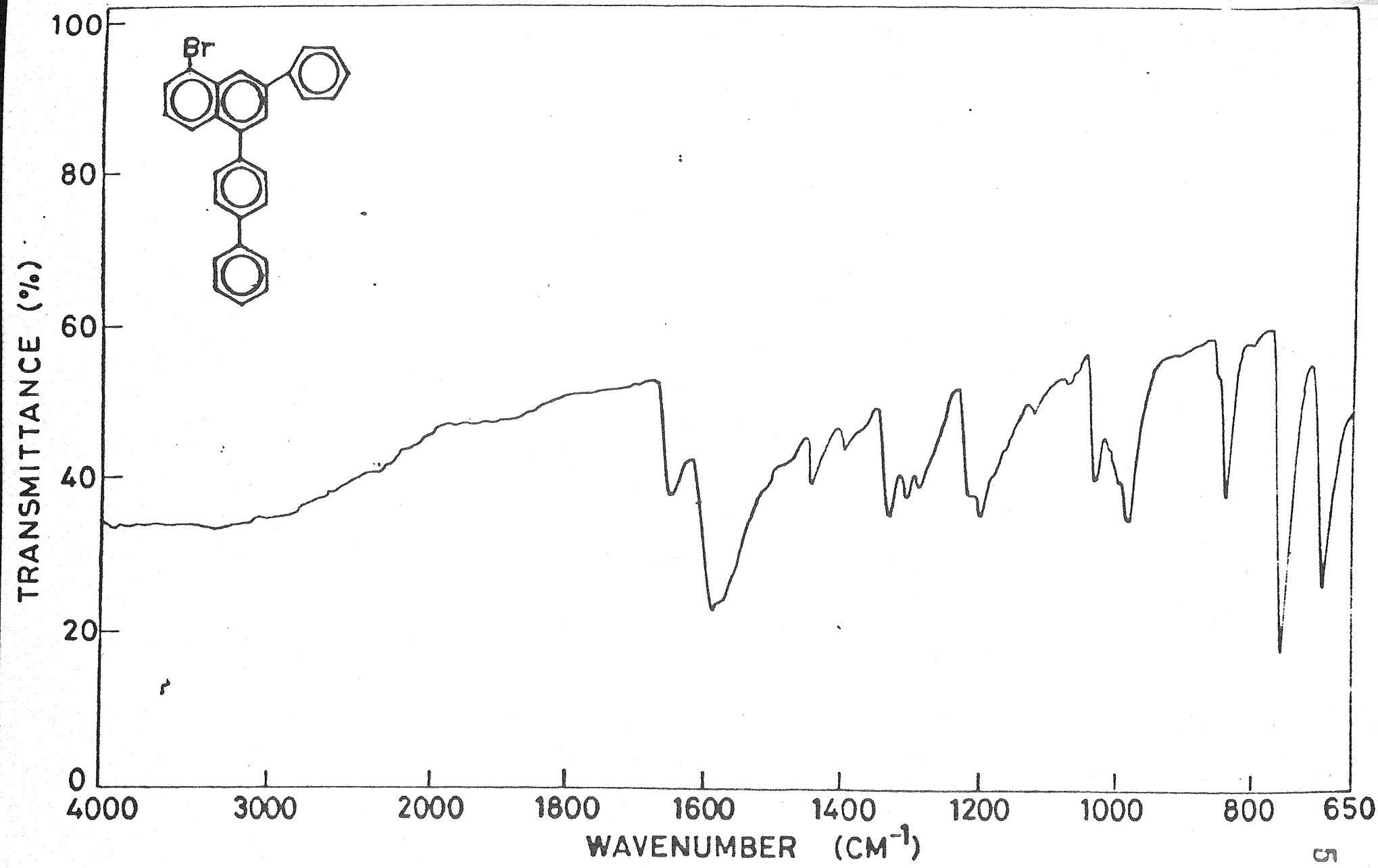


FIG. II · 8 IR SPECTRUM OF COMPOUND (211)

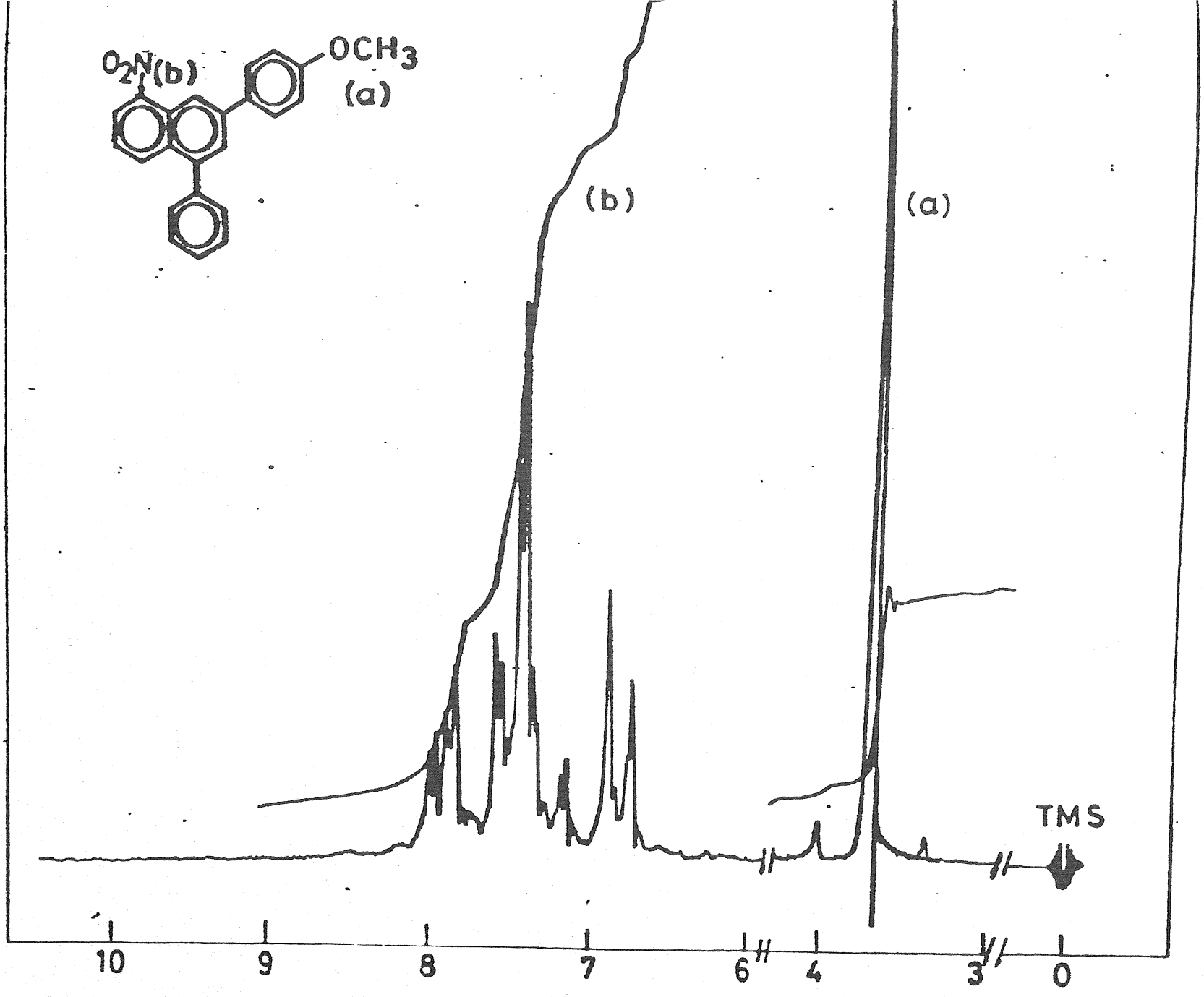


FIG II: 9 NMR SPECTRUM OF COMPOUND (22C)

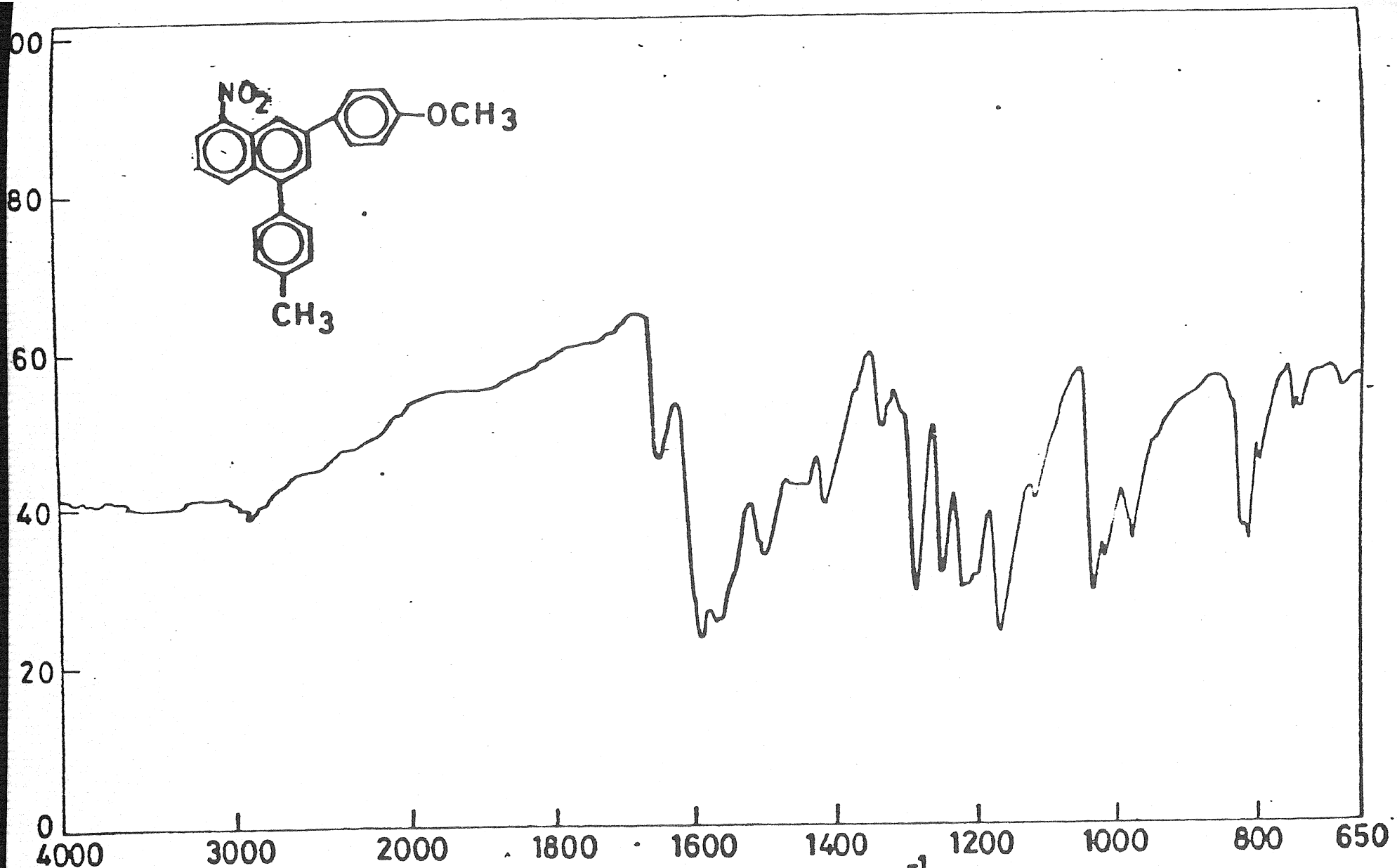


FIG. II. 10 I R SPECTRUM OF COMPOUND (22g)

toluenes at elevated temperatures[10,11].

The substituted benzylideneacetophenones (18) were prepared by a general procedure[12]. This method consists of stirring the equimolar quantities of aromatic aldehydes and methyl ketones in the presence of an alkali at 0°C. The resulting precipitate of α, β -unsaturated ketones was recrystallized from ethanol by benzene: Pet.ether (60-80°C) in 40-80% yields.

II.4.3. Prepration of O-chlorobenzyl dimethyl sulfonium bromide (16a) :

A solution of dimethyl sulfide (50 m mole) and O-chlorobenzyl bromide (50m mole) in 50 ml of anhydrous benzene was allowed to reflux on a water bath for 4 hrs. A solid mass was precipitated which was filtered, dried and recrystallized twice from chloroform, n-hexane to give white shining crystals of O-chlorobenzyl sulfonium bromide in 80% yields(11.50 gm) m.p.150-151°C (Lit[13] m.p.150-152°C).

IR data (KBr) Cm^{-1} : 3045(δ C-H to $CH_2-S^+<$)

NMR ($CDCl_3$) (δ ppm) : 5.10(s,2H, $-CH_2-S^+<$):

3.05(s,6H, di CH_3), 7.05-8.25(m,4H,ArH)

II.4.4. Prepration of O-bromobenzyl dimethyl sulfonium bromide (16b) :

O-bromobenzyl bromide (50m mole) and dimethyl sulfide

(50m mole) in anhydrous benzene (50 ml) was allowed to reflux on a water bath for 6 to 7 hrs. A solid mass was precipitated, which was filtered, dried and recrystallized twice from chloroform, ±n-hexane to give off white crystals of O-bromo-benzyldimethyl sulfonium bromide (16b) in 75% yields.

m.p.142-44°C (Lit[13] 144-145°C)

IR data (KBr) Cm^{-1} : 3040 (ν C-H to $-CH_2-S^+<$)

NMR ($CDCl_3$) (δppm) : 5.05 (s,2H, $CH_2-S^+<$)

3.00 (s,6H, di CH_3): 7.15-8.30(m,4H,ArH)

II.4.5. Prepration of O-nitrobenzyldimethyl sulfonium bromide (16c) :

A mixture containing (50m mole) of O-nitrobenzyl bromide and (50m mole) dimethyl sulfide in 50ml of anhydrous benzene was heated on a water bath for 8-10 hrs. Excess of solvent was evaporated and Pet.ether(60-80) was added to precipitate O-nitrobenzyl dimethyl sulfonium bromide (16c). This salt (16c) was twice crystallized from chloroform, n-hexane (1:2) to give a yellow crystalline compound m.p.158-60°C (Lit[14] m.p.155-60°C) yields26.5 gm (90%).

IR data (KBr)Cm^{-1} : 3040 (νC-H to $CH_2-S^+<$),

1520, 1300 (ν-NO_2)

NMR ($CDCl_3$) (δppm): 5.30 (s,2H, $CH_2-S^+<$)

3.20 (s,6H, di CH_3): 7.05-8.40(m,4H,ArH)

II.4.6. Prepration of 1,3-diaryl-5-chloronaphthalenes (20a-m) :

A mixture of O-chlorobenzyldimethyl sulfonium bromide (16a) (3m mole) and α,β -unsaturated ketones (3m mole) was stirred at 200°C in the presence of anhydrous zinc chloride (3.0g) in 10ml glacial acetic acid for 6-9 hrs under nitrogen atmosphere. Reaction mixture, after keeping overnight at room temperature into ice cold water (20ml) to precipitate a solid mass. The solid mass was separated by filteration, dried and subjected to column chromatography using neutral alumina as absorbent and chloroform as solvent. The products were recrystallized from suitable solvents to give better yields of the titled compounds (20a-m). Table (II.1). The NMR and IR spectral data of naphthalenes (20a-m) have been tabulated in table II 2-3.

II.4.7. Preparation of 1,3-diaryl-5-bromonaphthalenes (21a-m) :

Taking the (3m mole) solution of O-bromobenzyldimethyl sulfonium bromide (16b) in a 100ml round bottom flask and equipped with a reflux condenser with magnetic stirrer and α,β -unsaturated ketones in 5.0ml of glacial acetic acid followed by the addition of 3-0gm anhydrous zinc chloride. The mixture was stirred at 200°C for 6-8 hrs under an inert atmosphere of nitrogen. The resulting solution was allowed to stand overnight at room temperature. Ice cold water (20ml) was then added, the

precipitate so obtained was filtered off, dried and chromatographed over neutral alumina chloroform fraction which on crystallization from an appropriate solvent gave a fine crystalline solid due to formation of 1,3-diaryl O-bromonaphthalenes (21a-m).

All the naphthalene derivatives (21a-m) were prepared using the same general procedure. Their physical constants are listed in table II.1-3.

II.4.8. Preparation of 1,3-diaryl-5-nitronaphthalenes (22a-m) :

In a 100ml round bottom flask, equipped with a reflux condenser and a magnetic stirrer, was placed with a solution of O-nitrobenzyl dimethyl sulfonium bromide (16c)(3m mole) and α, β -unsaturated ketones in 5.0ml of glacial acetic acid followed by the addition of 3.0gm anhydrous zinc chloride. The mixture was stirred at 200°C for 7-9 hrs under an inert atmosphere of nitrogen. The resulting solution was allowed to stand over night at room temperature. Ice cold water (20ml) was then added. The precipitate so obtained, was filtered off, dried and chromatographed over neutral alumina chloroform fraction which on crystallization from an appropriate solvent gave an appropriate solvent gave a fine crystalline solid due to formation of 1,3-diaryl-O-nitronaphthalenes (22a-m).

All the naphthalenes derivatives (20a-22m) were

prepared using the same general procedure. Their physical constants are listed in table II.1-3.

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TABLE II.1. PHYSICAL PROPERTIES OF NAPHTHALENES DE IVATIVES(20a-22m)

Compound	X	Ar^1	Ar^2	Yield %	m.p. ^oC	Lit.[6] m.p. ^oC	Recry-stn. solvent	Anal.data found/(Calcd.) C %	H %
1	2	3	4	5	6	7	8	9	10
20a	Cl	C_6H_5	C_6H_5	50	92-94	94-96	B	83.82 (83.94)	4.83 (4.77)
b	Cl	C_6H_5	$4\text{-}CH_3C_6H_4$	50	109-11	108-10	C	84.04 (84.02)	5.14 (5.18)
c	Cl	C_6H_5	$4\text{-}CH_3\cdot OC_6H_4$	54	124-26	125-27	A	80.18 (80.12)	4.82 (4.93)
d	Cl	C_6H_5	$4\text{-}Cl.C_6H_4$	56	108-10	110-12	C	75.61 (75.64)	4.07 (4.01)
e	Cl	C_6H_5	$3,4\text{-}O_2CH_2\cdot C_6H_3$	55	134-36	133-35	C	77.38 (74.42)	3.70 (3.65)
f	Cl	$4\text{-}CH_3\cdot C_6H_4$	C_6H_5	67	120-21	121-22	A	84.05 (84.02)	5.06 (5.14)
g	Cl	$4\text{-}CH_3\cdot C_6H_4$	$4\text{-}CH_3O.C_6H_4$	52	96-98	95-97	B	80.28 (80.33)	5.32 (5.30)
h	Cl	$4\text{-}Cl.C_6H_4$	$4\text{-}NO_2\cdot C_6H_4$	55	192-94	190-91	B	69.90 (69.84)	3.50 (3.44)
i	Cl	$2\text{-}C_{10}H_7$	C_6H_5	60	170-72	170-72	C	85.57 (85.60)	4.59 (4.66)
j	Cl	$1\text{-}C_{10}H_7$	$4\text{-}Cl.C_6H_4$	62	173-74	171-74	A	78.25 (78.20)	4.07 (4.01)

CONTD.Table II.1.

1	2	3	4	5	6	7	8	9	10
k	Cl	2-$C_{10}H_7$	3-CH_3.C_6H_4	57	189-91	190-92	B	85.53 (85.60)	5.08 (5.02)
l	Cl	4-C_6H_5.C_6H_4	C_6H_5	55	162-64	160-62	C	86.07 (86.04)	4.78 (4.87)
m	Cl	2-C_4H_3S	4-CH_3O.C_6H_4	62	173-74	172-73	A	71.80 (71.90)	4.33 (4.28)
21a	Br	C_6H_5	C_6H_5	58	92-93	94-96	B	73.40 (73.53)	4.45 (4.56)
b	Br	C_6H_5	4-CH_3.C_6H_4	60	113-15	112-14	A	73.90 (73.99)	4.50 (4.56)
c	Br	C_6H_5	4-CH_3O.C_6H_4	65	124-26	126-28	C	70.05 (70.95)	4.32 (4.37)
d	Br	C_6H_5	4-Cl.C_6H_4	62	115-16	114-16	B	67.15 (67.09)	3.65 (3.56)
e	Br	C_6H_5	3,4-O_2CH_2.C_6H_3	64	131-33	132-34	A	68.56 (68.49)	3.80 (3.72)
f	Br	4-$CH_3C_6H_4$	C_6H_5	68	118-20	120-22	C	74.65 (74.59)	3.85 (3.78)
g	Br	4-$CH_3C_6H_4$	4-CH_3O.C_6H_4	54	98-100	96-98	B	71.40 (71.46)	4.73 (4.71)
h	Br	4-Cl.C_6H_4	4-NO_2.C_6H_4	52	190-92	189-91	C	62.23 (62.27)	2.85 (2.81)
i	Br	2-$C_{10}H_7$	C_6H_5	49	172-74	174-76	A	76.29 (76.28)	4.14 (4.16)

CONTD. Table II.1.

1	2	3	4	5	6	7	8	9	10
j	Br	2-$C_{10}H_7$	4-Cl.C_6H_4	70	175-77	176-78	B	70.38 (70.35)	3.58 (3.61)
k	Br	1-$C_{10}H_7$	3-CH_3.C_6H_4	52	192-94	191-93	B	76.58 (76.60)	4.48 (4.49)
l	Br	4-C_6H_5.C_6H_4	C_6H_5	50	161-63	162-64	A	77.20 (77.24)	4.38 (4.36)
m	Br	2-C_4H_3S	4-CH_3O.C_6H_4	54	172-74	174-76	C	55.54 (55.58)	3.25 (3.26)
22a	NO_2	C_6H_5	C_6H_5	55	91-93	94	A	81.14 (81.20)	4.63 (4.61)
b	NO_2	C_6H_5	4-CH_3.C_6H_4	68	110-112	112	B	81.91 (81.89)	5.03 (5.01)
c	NO_2	C_6H_5	4-CH_3O.C_6H_4	62	132-34	128-30	C	77.58 (77.74)	4.73 (4.78)
d	NO_2	C_6H_5	4-Cl.C_6H_4	70	111-13	115	B	73.90 (73.99)	3.82 (3.89)
e	NO_2	C_6H_5	3,4-O_2CH_2.C_6H_3	65	132-34	133	A	74.75 (74.80)	4.10 (4.06)
f	NO_2	4-CH_3.C_6H_4	C_6H_5	55	120-22	118-20	B	81.35 (81.41)	5.04 (5.01)
g	NO_2	4-CH_3.C_6H_4	4-CH_3O.C_6H_4	65	94-96	96	A	78.12 (78.10)	5.16 (5.14)

CONTD. Table II.1.

1	2	3	4	5	6	7	8	9	10
h	NO_2	4-Cl.C_6H_4	4-NO_2.C_6H_4	68	190-91	188	B	66.14 (66.00)	3.27 (3.25)
i	NO_2	2-$C_{10}H_7$	C_6H_5	58	173	171-72	A	83.30 (83.20)	4.61 (4.55)
j	NO_2	2-$C_{10}H_7$	4-Cl.C_6H_4	72	176-77	178	B	76.14 (76.19)	3.92 (3.90)
k	NO_2	2-$C_{10}H_7$	3-CH_3.C_6H_4	52	189-91	192-94	C	82.63 (82.53)	5.27 (5.29)
l	NO_2	4-C_6H_5.C_6H_4	C_6H_5	47	164-66	165	B	83.70 (83.79)	4.76 (4.73)
m	NO_2	2-C_4H_3S	4-CH_3O.C_6H_4	58	176-78	177	C	77.03 (79.74)	5.04 (5.06)

A = Benzene: Pet.Ether

B = Chloroform: Pet.ether

C = Benzene: Chloroform.

TABLE II.2. IR DATA (KBr) Cm^{-1} OF NAPHTHALENES

Compound	IR Data (KBr) Cm^{-1}				
	νC-H	νC=C	ϕC-H	νC-NO_2	νC-X(Cl,Br)
20a	3030	1595	990	-	780
b	3045	1595	995	-	775
c	3080	1598	992	-	785
d	3110	1610	995	-	780
e	3120	1605	992	-	782
f	3075	1605	995	-	788
g	3060	1585	992	-	782
h	3068	1610	995	1505, 1335	790
i	3075	1615	990	-	795
j	3090	1612	995	-	798
k	3070	1605	990	-	790
l	3095	1600	992	-	775
m	3100	1605	990	-	780
21a	3045	1610	995	-	695
b	3050	1600	990	-	710
c	3085	1605	985	-	705
d	3095	1595	995	-	720
e	3105	1610	990	-	700
f	3130	1605	1005	-	695
g	3085	1615	995	-	685

CONTD. Table II.2.

1	2	3	4	5	6
h	3105	1608	998	1505, 1340	695
i	3085	1600	990	-	780,690
j	3065	1595	995	-	695
k	3095	1610	1000	-	700
l	3075	1605	998	-	675
m	3110	1610	995	-	695
22a	3095	1605	992	1500, 1330	-
b	3090	1608	998	1515, 1335	-
c	3100	1615	990	1520, 1325	-
d	3070	1605	992	1510, 1320	-
e	3090	1595	990	1505, 1310	-
f	3105	1605	995	1505, 1345	-
g	3122	1605	992	1500, 1340	-
h	3145	1618	988	1510, 1325	-
i	3110	1605	996	1515, 1335	-
j	3105	1610	992	1525, 1335	-
k	3115	1600	982	1505, 1310	-
l	3060	1598	990	1500, 1325	-
m					

ν = Stretching vibrations ϕ = Out of the plane deformations of hydrogen attached to aromatic nucleus.

TABLE II.3. NMR ($CDCl_3$) DATA OF NAPHTHALENE DERIVATIVES(20a-22m).

Compound	δ(ppm)	No.of protons	Assignment of protons
1	2	3	4
20a	-	-	-
b	2.50, s	3H	CH_3
	6.92-8.22, m	14H	Phenyl+naphthyl
c	3.80, s	3H	OCH_3
	6.82-8.24, m	14H	Phenyl+naphthyl
d	-	-	-
e	6.05, s	2H	$-O_2CH_2$
	6.72-8.15, m	13H	Phenyl+naphthyl
f	2.45, s	3H	CH_3
	6.80-8.15, m	14H	Phenyl+naphthyl
g	3.75, s	3H	OCH_3
	2.35, s	3H	CH_3
	6.85-8.06, m	13H	Phenyl+naphthyl
i	-	-	-
j	-	-	-
k	2.35, s	3H	CH_3
	6.80-8.25, m	16H	Phenyl+naphthyl
m	3.80, s	3H	OCH_3
	6.88-8.20, m	12H	Phenyl+naphthyl

CONTD. Table II.3.

1	2	3	4
21a	-	-	-
b	2.40, s	3H	CH_3
	6.85-8.25, m	14H	Phenyl+naphthyl
c	3.75, s	3H	OCH_3
	6.75-8.20, m	14H	Phenyl+naphthyl
d	-	-	-
e	6.00, s	2H	O_2CH_2
	6.65-8.10, m	13H	Phenyl+naphthyl
f	2.40, s	3H	CH_3
	6.75-8.10, m	14H	Phenyl+naphthyl
g	3.70, s	3H	OCH_3
	2.30, s	3H	CH_3
	6.80-8.20, m	13H	Phenyl+naphthyl
h	-	-	-
i	-	-	-
j	-	-	-
k	2.45, s	3H	CH_3
	6.80-8.20, m	16H	Phenyl+naphthyl
l	-	-	-
m	3.70, s	3H	OCH_3
	6.65-8.10, m	12H	Phenyl+naphthyl

CONTD. Table II.3.

1	2	3	4
22a	-	-	-
b	2.48, s	3H	CH_3
	6.95-8.30, m	14H	Phenyl+naphthyl
c	3.87, s	3H	OCH_3
	6.87-8.29, m	14H	Phenyl+naphthyl
d	-	-	-
e	6.03, s	2H	$-O_2CH_2-$
	6.72-8.15, m	13H	Phenyl+naphthyl
f	2.33, s	3H	CH_3
	6.77-8.18, m	14H	Phenyl+naphthyl
g	2.35, s	3H	CH_3
	3.75, s	3H	OCH_3
	6.80-8.21, m	13H	Phenyl+naphthyl
h	-	-	-
i	-	-	-
j	-	-	-
k	2.36, s	3H	CH_3
	6.82-8.30, m	16H	Phenyl+naphthyl
l	-	-	-
m	3.82, s	3H	OCH_3
	6.84-8.26, m	12H	Phenyl+naphthyl +thiophenyl

s = singlet m = multiplet

CHAPTER III

CHAPTER-III

SYNTHESIS OF SOME NEW 2,4,6-TRIARYL SUBSTITUTED PYRIDINES: USING STABILIZED π-SULFURANES : REACTION OF 4-METHOXY PHENACYLDIMETHYL SULFONIUM YLIDE WITH α, β -UNSATURATED KETONES:

III.1. ABSTRACT :

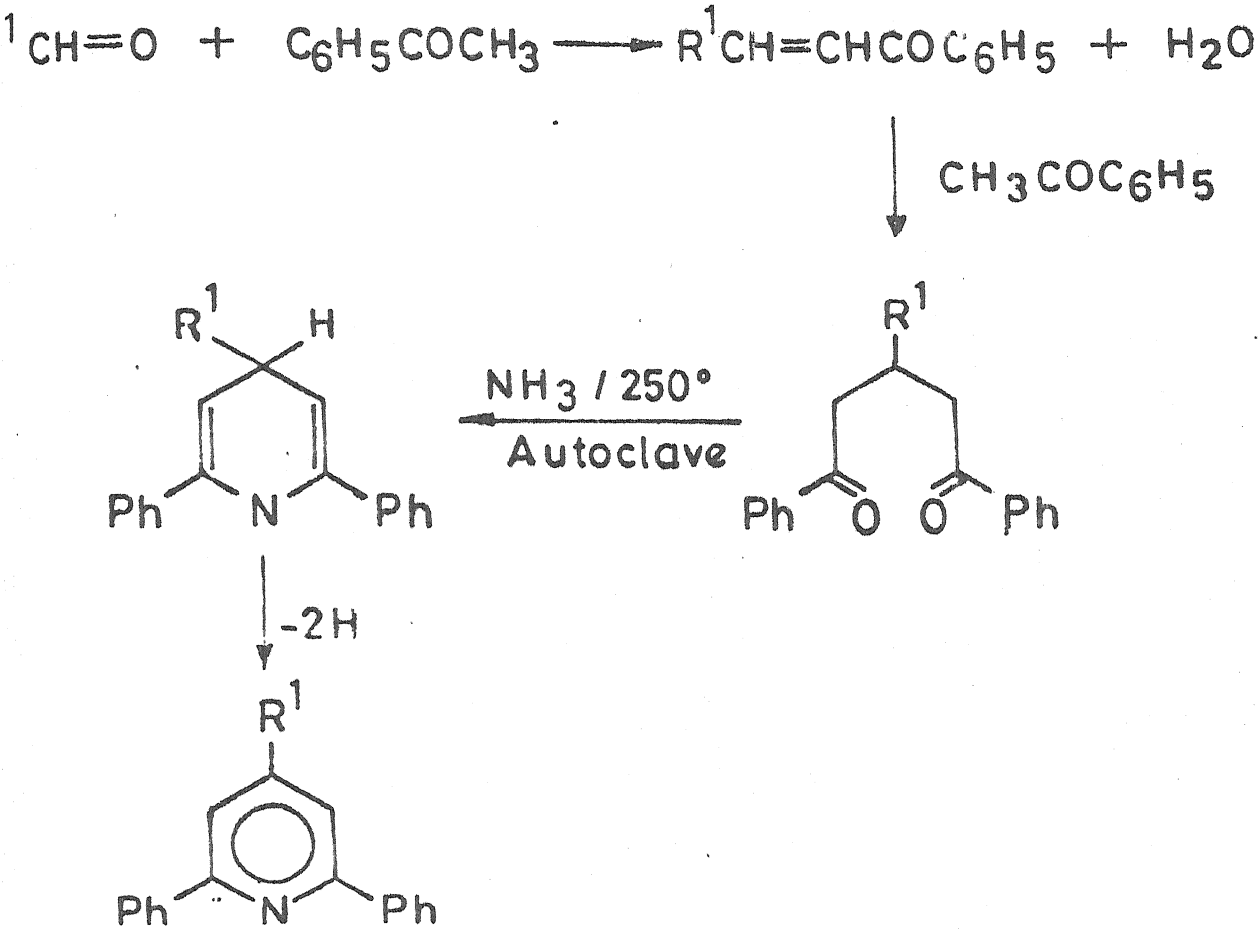
A 4-methoxyphenacyldimethyl sulfonium bromide was prepared by heating 4-methoxyphenacyl bromide and dimethyl sulfide in benzene or acetone at reflux temperature. The sulfonium salt on treatment with aq.NaOH in methanolic solution gave 4-methoxyphenacylidene dimethyl sulfurane. The salt or ylide on reaction with α, β -unsaturated ketones in presence of ammonium acetate in acetic acid or methanol gave asymmetrical pyridines having different substituents at 2,4,6-positions. Similarly, when the salt or ylide was reacted with 4-methoxyacetophenones in presence of ammonium acetate, 2,6-di (4-methoxyphenyl)4-arylpyridines having identical substituents at C_2 and C_6 position was formed. Attempts to synthesize symmetrical pyridines having identical substituents at 2,4,6 position involved the condensation of salt or ylide with 4-methoxy benzal-4-methoxyacetophenone in ammonium acetate in acetic acid. All pyridines were confirmed by IR and NMR spectral data.

III.2. INTRODUCTION :

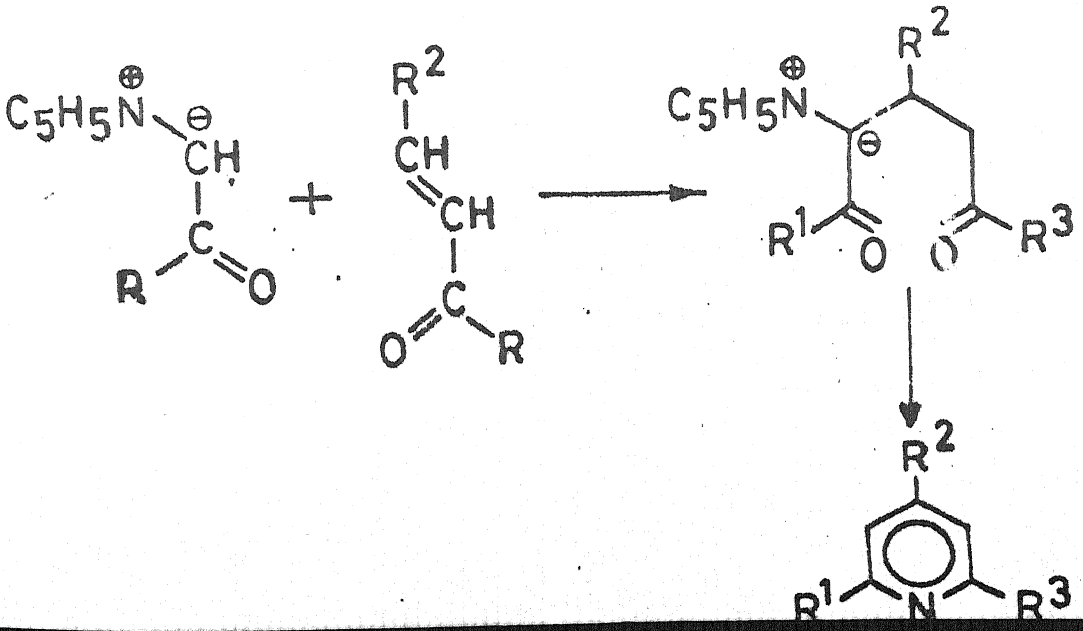
On the earlier methods involving aza ring closure leading to the synthesis of substituted pyridines was first reported by Tschitschibabin[1]. The method involved the condensation of aldehyde and methyl ketone in presence of liquid ammonia (Scheme III.1). But this method was not versatile because of harsh reaction conditions and poor yields of products. Subsequent to this report, Frank et al[2,3] made an improvement over the earlier reported method by using ammonia and catalytic amount of ammonium acetate.

Later on Krohnke et al[4,5] developped a superior method, involving the interaction of pyridinium salts or ylides with α,β -unsaturated ketones (Scheme III.2). The course of the reaction involves the same pantan-1,5-dionyl intermediate, analogous to the diketone intermediate formed in earlier methods. The intermediate undergoes aza ring closure with ammonium acetate in glacial acetic acid to give 2,4,6-triaryl pyridines. The superiority of Krohnke's method[4,5] over Tschitschibabin's method[1] lies in the requirement of mild reaction conditions and better yields of pyridines. Moreover, earlier methods[1,3] were restricted to the prepration of symmetrical pyridine having identical substituents at 2 & 6 positions of pyridine ring. The Krohnke's[4,5] method allows the synthesis of both symmetrical and asymmetrical pyridine

Scheme III·1



Scheme III·2



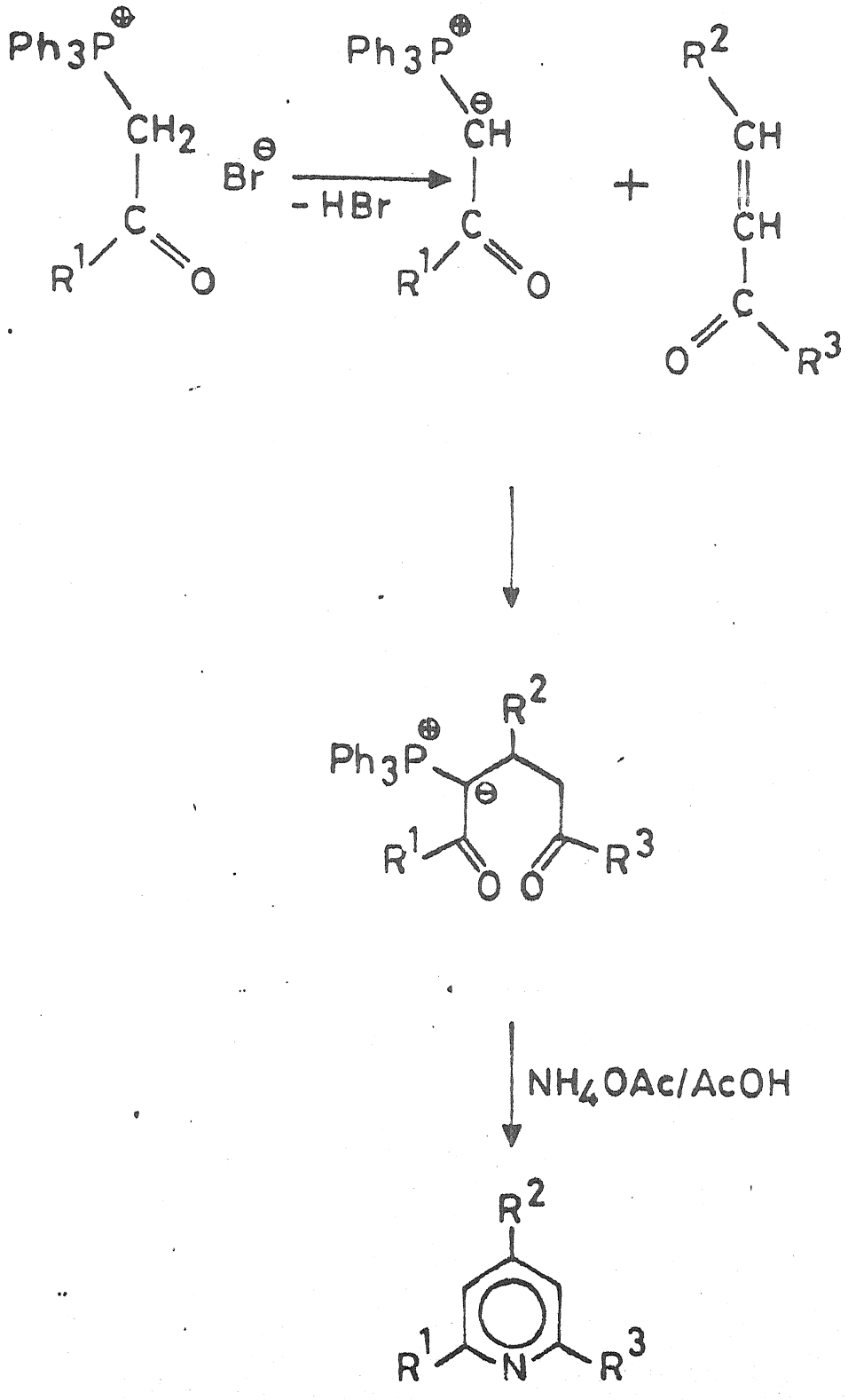
having different substituents at 2,4,6-positions of pyridines nucleus.

After the report of Krohnke[4,5], several pioneer workers reported[6-9] the synthesis of new 2,4,6-triaryl pyridines using phenacyl pyridinium ylides or salts with a view to test the domain of the applicability of the reaction.

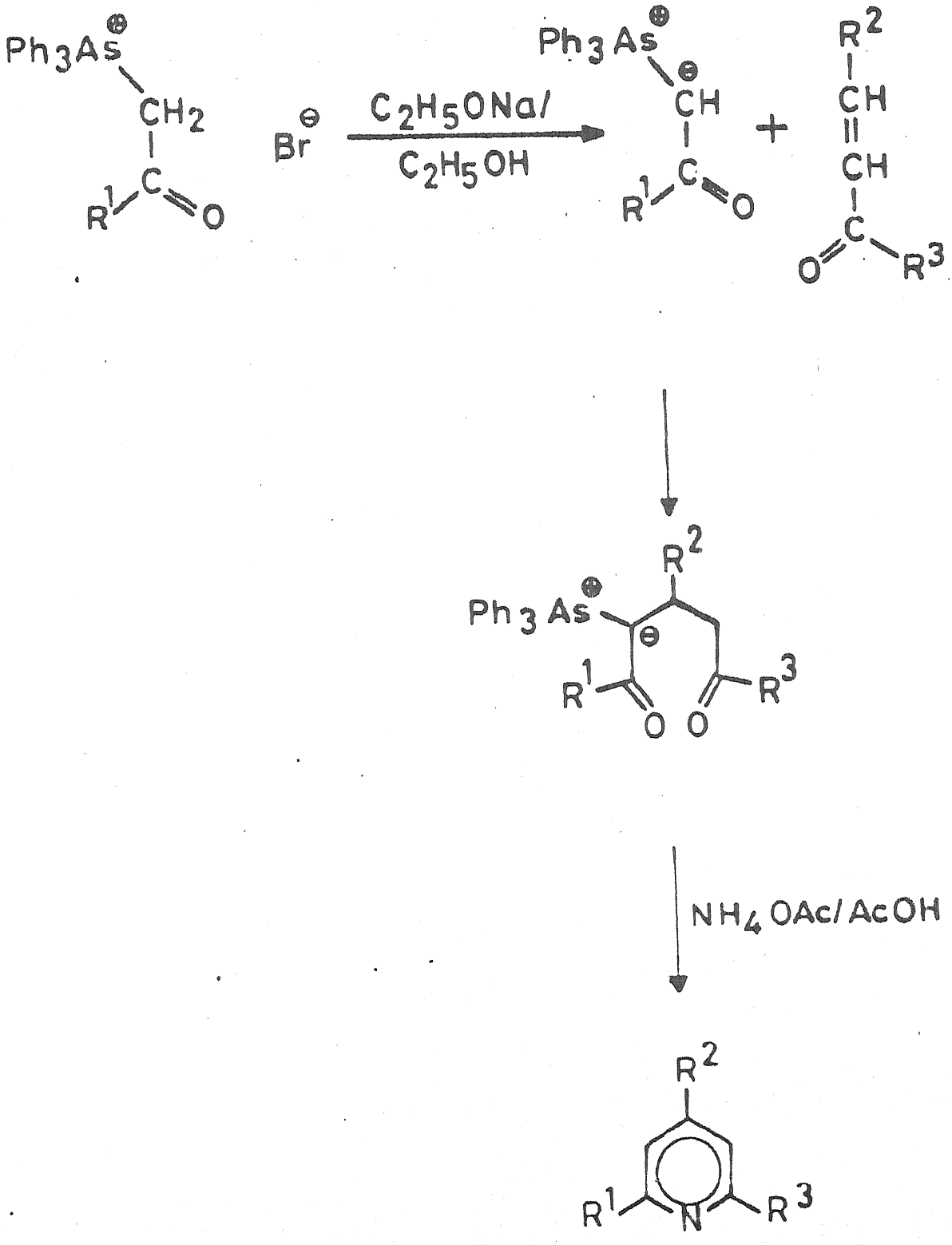
Recently phosphonium[10] (Scheme III.3) and Arsonium[11] (Scheme III.4) ylides are also reported to couple with α, β - unsaturated ketones in presence of ammonium acetate leading to the synthesis of pyridine nucleus analogous to the corresponding pyridinium ylide and follows the similar course of reaction as reported for pyridinium ylide. But these routes[10] for the prepration of pyridine nucleus were not much facile as it involved the separation of leaving group triphenyl-phosphine or triphenyl arsine from the reaction mixture whereas in the former method[4,9] leaving group was washed out.

Literature reveals that sulfonium ylides and their precursors have been used in the synthesis of a large variety of cyclic and heterocyclic systems viz.cyclopropanes[12,13], epoxides[14], indoles[15,16], aziridines[17] and tetrazines[18]. Tewari et al[19] in a few reactions reported that sulfonium salt or ylide also under went aza ring closure reaction leading to the synthesis of pyridine nucleus. But the domain of the applicability of this reaction could not be duplicated

SCHEME III·3


Ph3P⊕
CH2
C
R1
O
Br⊖
- HBr
Ph3P⊕
⊖CH
C
R1
O
+
R2
CH
CH
C
O
R3
R2
Ph3P⊕
⊖
R1
O
O
R3
NH4OAc/AcOH
R2
R1
N
R3

SCHEME III.4


Ph3As⊕
CH2
C
R1
O
Br⊖
C2H5ONa/
C2H5OH
Ph3As⊕
⊖
CH
C
R1
O
+
R2
CH
CH
C
O
R3
R2
Ph3As⊕
⊖
R1
R3
O O
NH4OAc/AcOH
R2
R1
N
R3

until recently.

Therefore, it seemed to be pertinent to elaborate some more reactions of sulfonium salts and their π-sulfuranes with a view to test the domain of synthetic applicability. In the present chapter, we have reported the synthesis of some asymmetrical and symmetrical methoxypyridines having various different substituents by the condensation of p-methoxy phenacylidinedimethyl sulfurane with a wide variety of α, β-unsaturated ketones in presence of ammonium acetate in acetic acid.

III.3. RESULTS AND DISCUSSION :

Condensation of 4-methoxyphenacyl bromide prepared by the bromination of 4-methoxy acetophenone with DMS gave 4-methoxyphenacyldimethyl sulfonium bromide(1). The structure of salt (1) was evidenced by IR and NMR spectral data. The IR spectrum of salt (1) displayed a strong band at 1675 Cm^{-1} due to C=O. The NMR spectrum showed a strong singlet at δ3.05 due to two methyl groups directly linked to sulfonium group. A sharp singlet at δ5.35 revealed the methylene protons adjecent to the sulfonium group. The methoxy group appeared at δ3.75 and aromatic protons were observed in the range δ7.15-7.80.

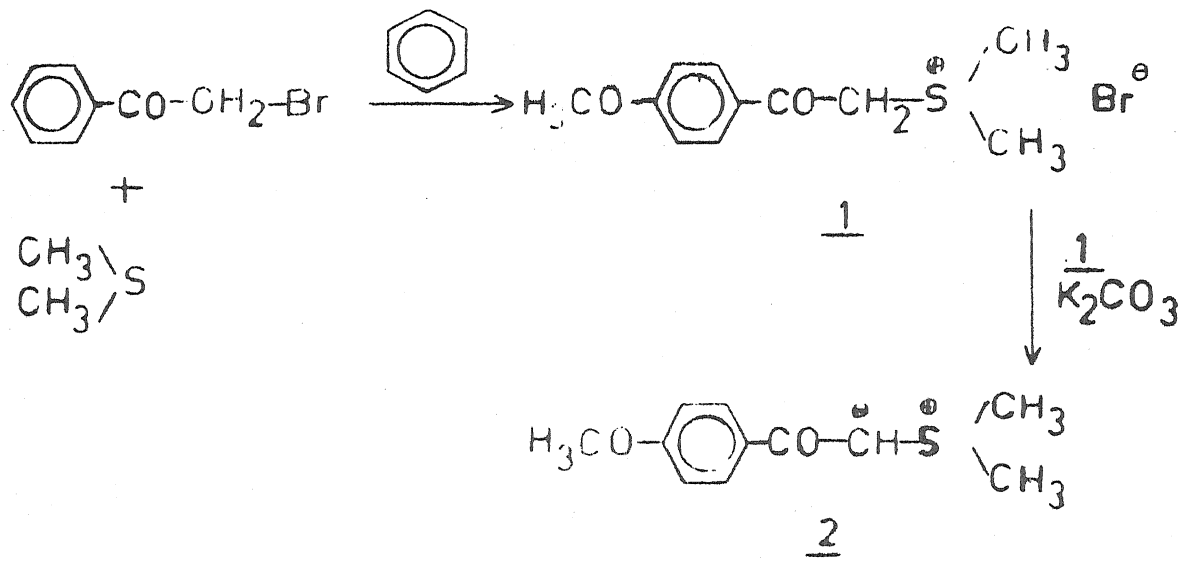
Salt (1) on treatment with aq.NaOH generated a yellow colouration which was changed into orange colour clearly

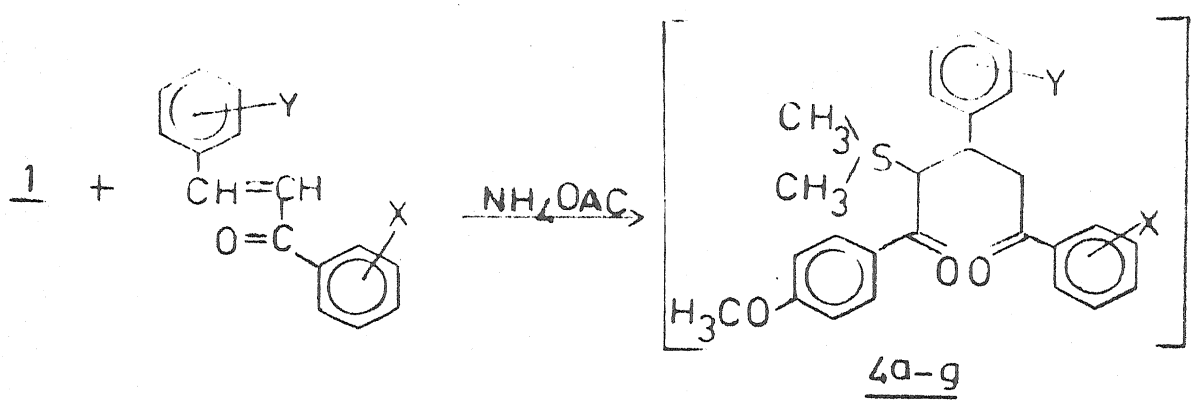
indicating the formation of ylide 4-methoxyphenacyldimethyl sulfurane (2). The (2) was isolated in the form of yellowish orange crystals owing to resonance stabilizing factors. The structures of ylide (2) was confirmed on the basis of IR and NMR spectral data. The IR spectrum showed a band of medium intensity in the region 1520 Cm^{-1} due to C-O stretching vibrations. This absorption is diagnostic of enolate structure. The NMR spectrum showed a singlet at δ3.15 due to two methyl protons. A methine proton adjecent to sulfonium group was observed at δ4.20. The aromatic multiplet was observed in the region δ7.20-8.15.

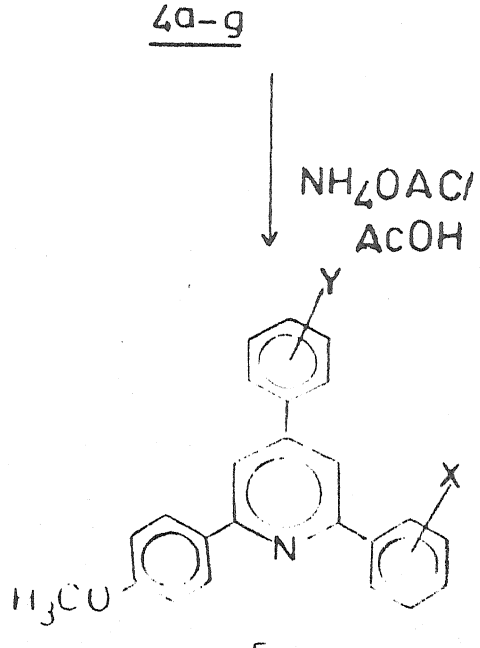
Ylide (2) so generated was though isolable but could not be strored for quite long time owing to its suscptibility towards atmospheric components and therefore, it was difficult to use ylide as starting material in the pyridine synthesis. Therefore salt (1) was used in the reaction and ylide (2) was generated in situ from its salt(1). Heating the mixture of salt (1) with α, β -unsaturated ketones (3a-r) in presence of ammonium acetate and glacial acetic acid gave 2,4,6-triarylpyridines (5a-r) in 45-70% yields(Scheme III.5).

Similarly, symmetrical pyridines 2,6-di(4-methoxyphenyl)-4-arylpyridines (5f-i) were also synthesized in 40-70% yields by the reaction of salt with substituted benzylidene-4-methoxy acetophenones (3f-i) in a mixture of ammonium acetate and acetic acid(Scheme III.6).

Scheme III.5





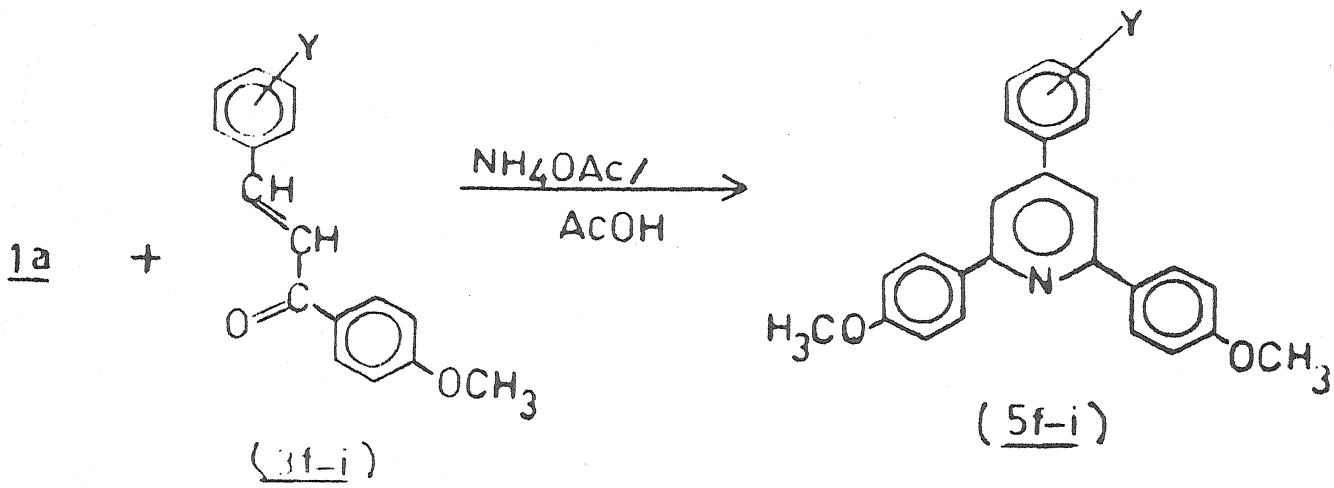


Next attention was towards the synthesis of pyridine (5c) having identical substituents at 2,4,6-positions of pyridine nucleus. This was achieved by heating salt (1) with 4-methoxybenzylidene-4-methoxy acetophenone (31) in presence of ammonium acetate in acetic acid giving 50% yield(Scheme III.7).

The course of reaction seems to be proceeded by the attack of ylide carbanion (2) on β-carbon of α, β -unsaturated ketones (3) to form pentane-1,5-dionyl dimethyl sulfonium ylide intermediates (4a-r) which,in turn, undergo aza ring closure in presence of ammonium acetate to form 2,4,6-triarylpyridines (5a-r).

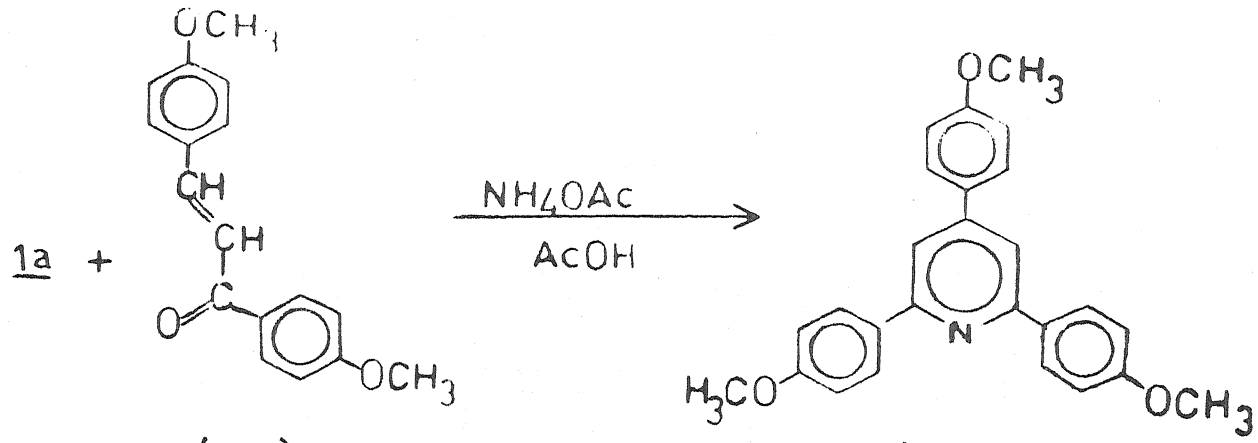
Various methoxypyridines (5a-r) prepared by the above method are listed in table III.1. All the pyridines gave satisfactory elemental analysis the melting point of the pyridines obtained by route abovesaid were very closed to that reported in literature[20]. The structures of pyridines were confirmed by spectral data[21]. The IR spectral data showed charecterstic absorption bands in the region 3050-3000Cm^{-1}, which were assigned to the C-H stretching mode of pyridine rings. Two bands the region 1600 and 1500 Cm^{-1} were due to the interaction between C=C and C=N vibrations of the pyridine rings. The NMR spectrum of the pyridines showed two pyridyl protons in the range δ6.35-6.65 and aromatic protons in the region δ6.40-8.05.

Scheme III.6



(3f-i) (5f-i)

Scheme.III.7



(3C) (5C)

III.4. EXPERIMENTAL :

Starting Material :

All the reagents obtained sources (E. Merck, B.D.H., SISCO, Polyform Fluka) starting materials were prepared according to the procedures reported in literature. 4-methoxy phenacyl bromide was prepared by the bromination of 4-methoxyacetophenone in either-dioxan method[22]. The benzylidene acetophenone were prepared by the condensation of substituted acetophenones with substituted benzaldehydes dissolved in alcohalic solution containing NaOH[23].

III.4.1. Prepration of 4-methoxyphenacyl dimethyl sulfonium bromide (1) :

Stirring a mixture of 4-methoxyphenacyl bromide (0.1 mole) and dimethyl sulfide (30ml) for 8 hrs gave white solid mass. The solid mass was filtered, washed twice with ether and recrystallized from alcohal as white colourless microcrystals m.p. 122-124°C (Lit.[20] 118-120°C).

IR Data (KBr) : 1675Cm^{-1} (ν C=O)

NMR ($CDCl_3$)Data (δ ppm) : 3.05(s, 6H, di CH_3) : 3.75(s, 3H, OCH_3) : 5.10(s, 2H, CH_2-S^{+}) : 7.08-8.22(m, 4H, ArH)

III.4.2. Prepration of 4-methoxyphenacylidine dimethyl sulfurane (2) :

4-Methoxyphenacyldimethylsulfonium bromide (1) (50m mole) was dissoved in water (30ml). The coloured suspension

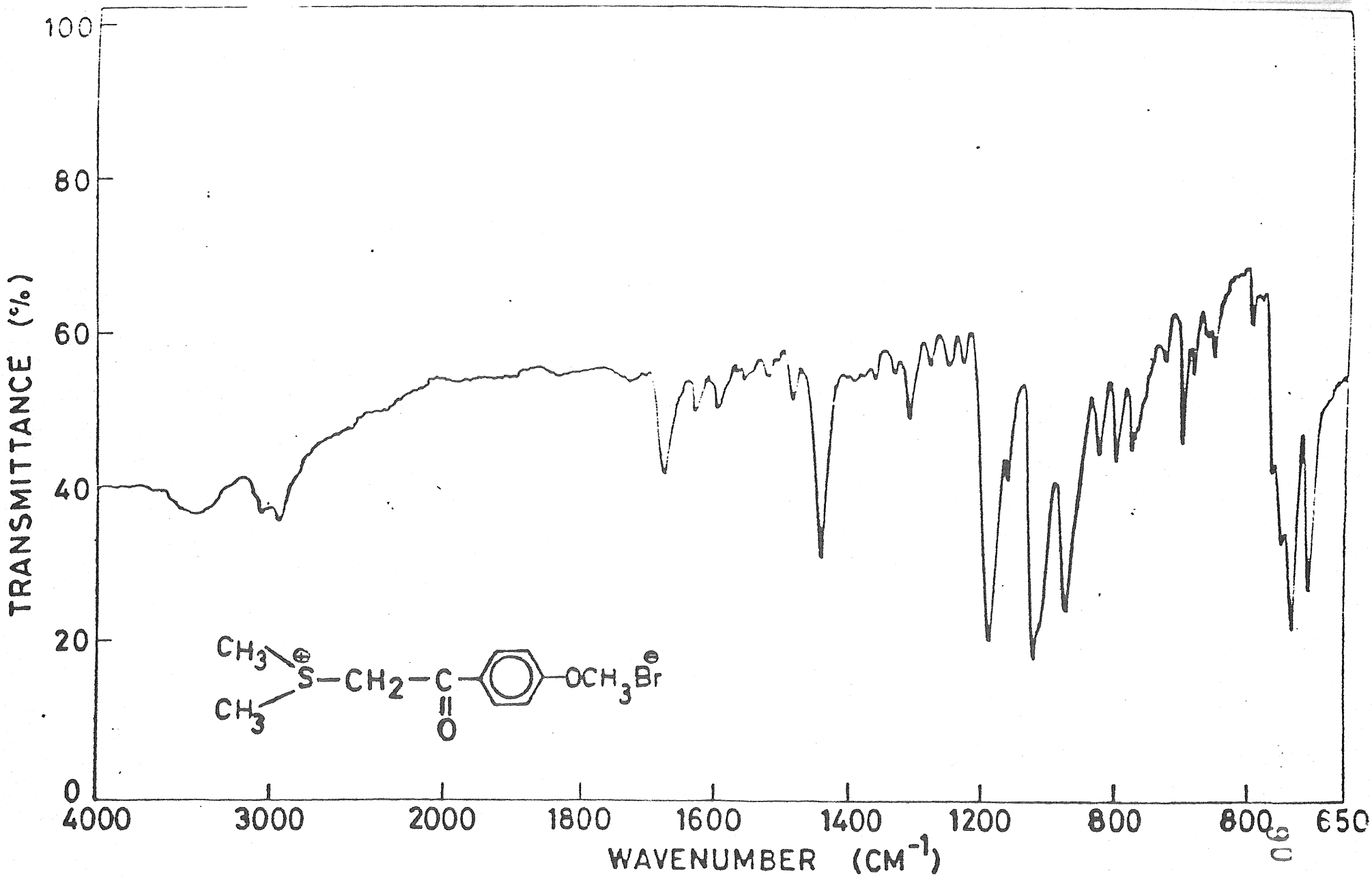


FIG. III·1 IR SPECTRUM OF SALT (1)

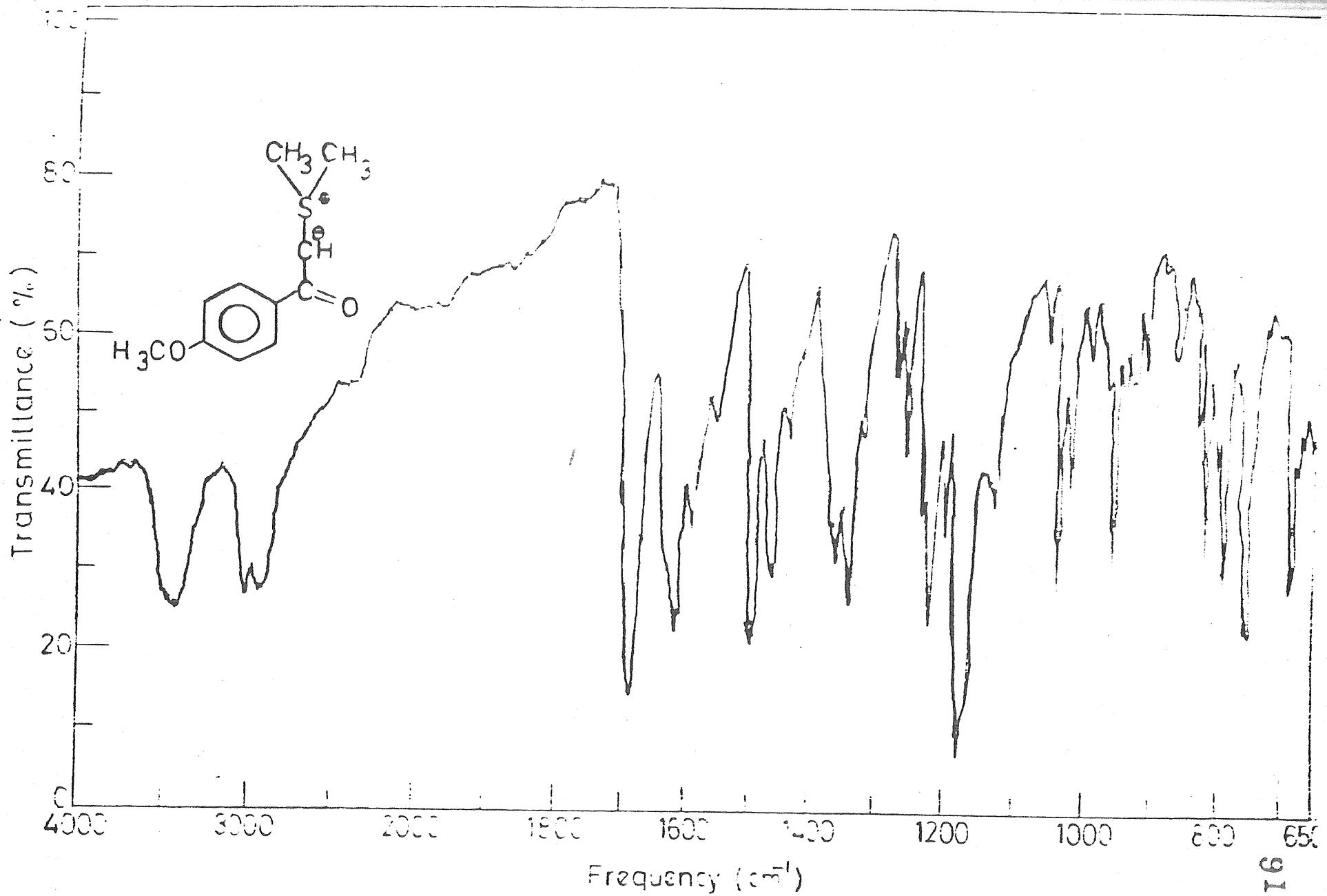


FIG III.2 IR SPECTRUM OF 2 . . .

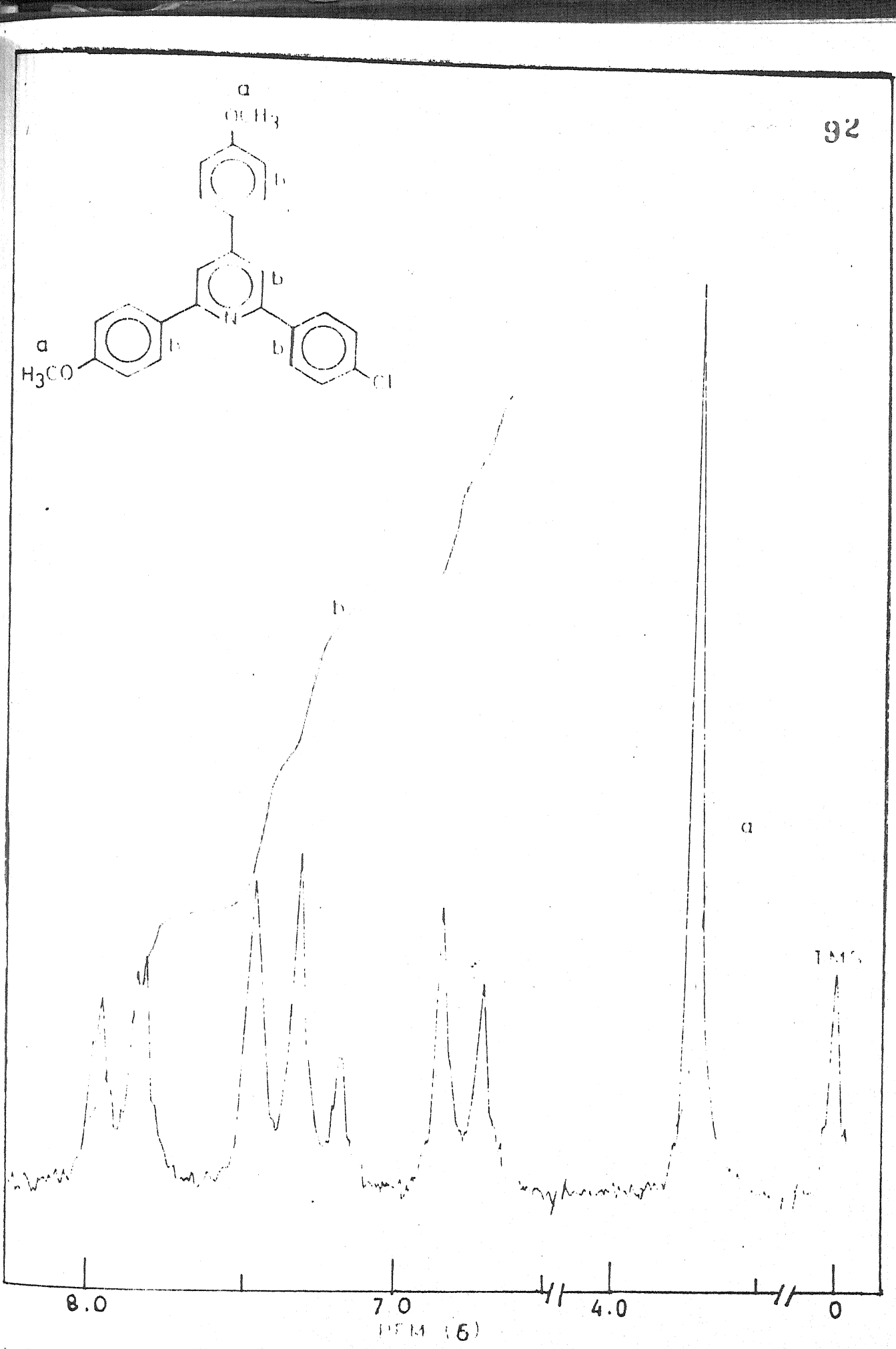


FIG. III. 3 NMR SPECTRUM OF 5a

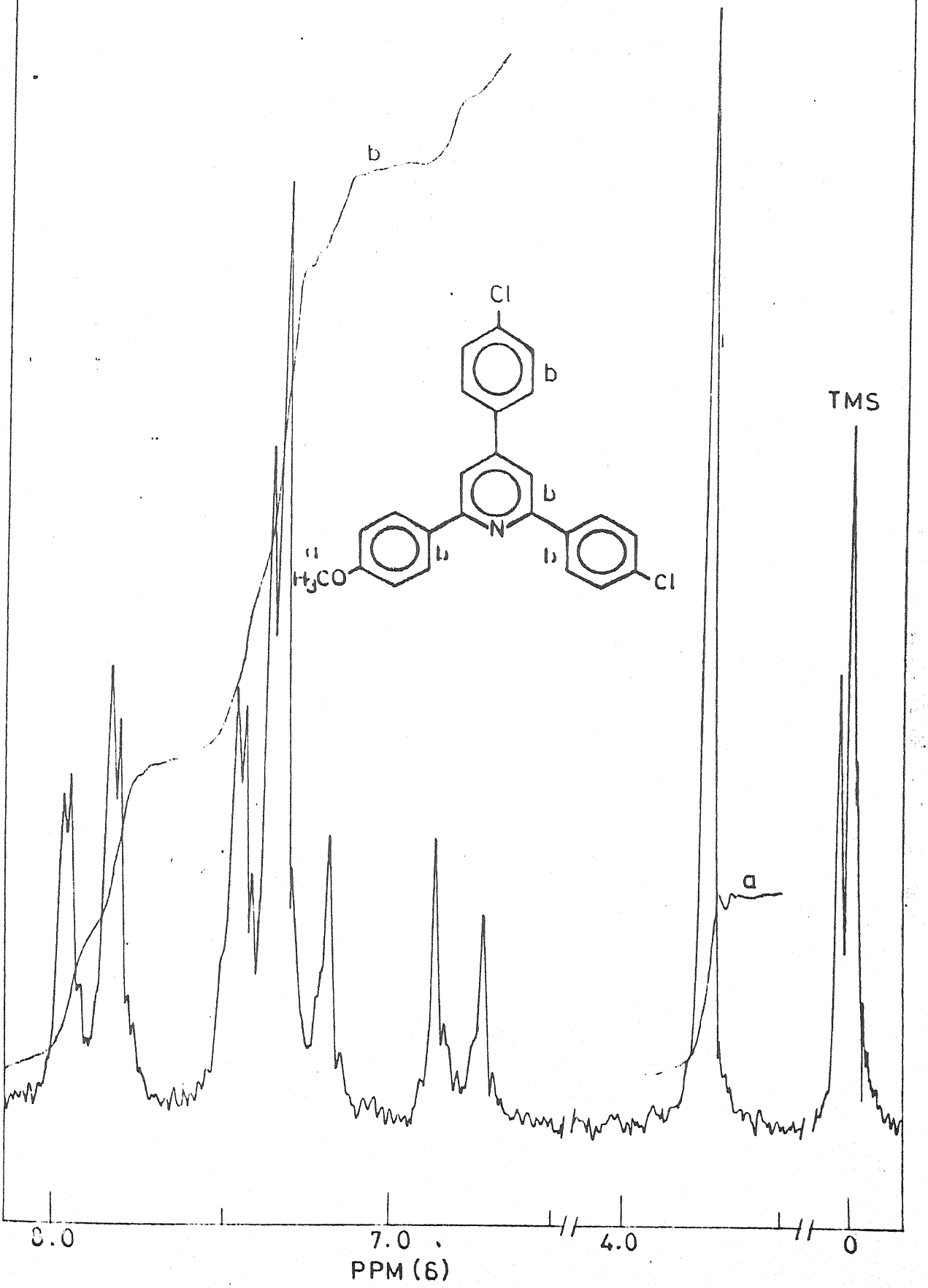
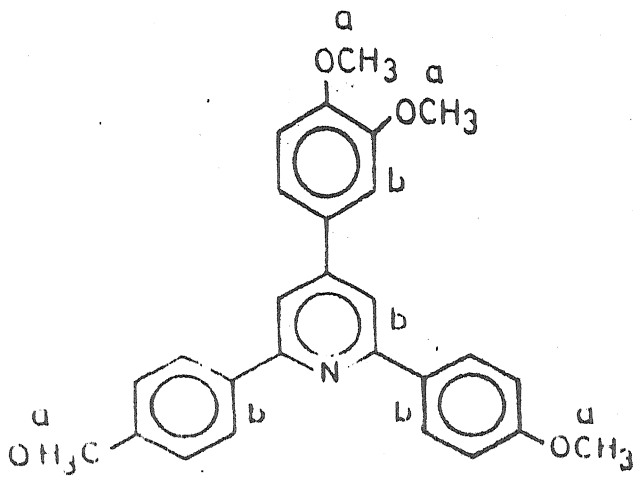


FIG. III.4 NMR SPECTRUM OF 5b .



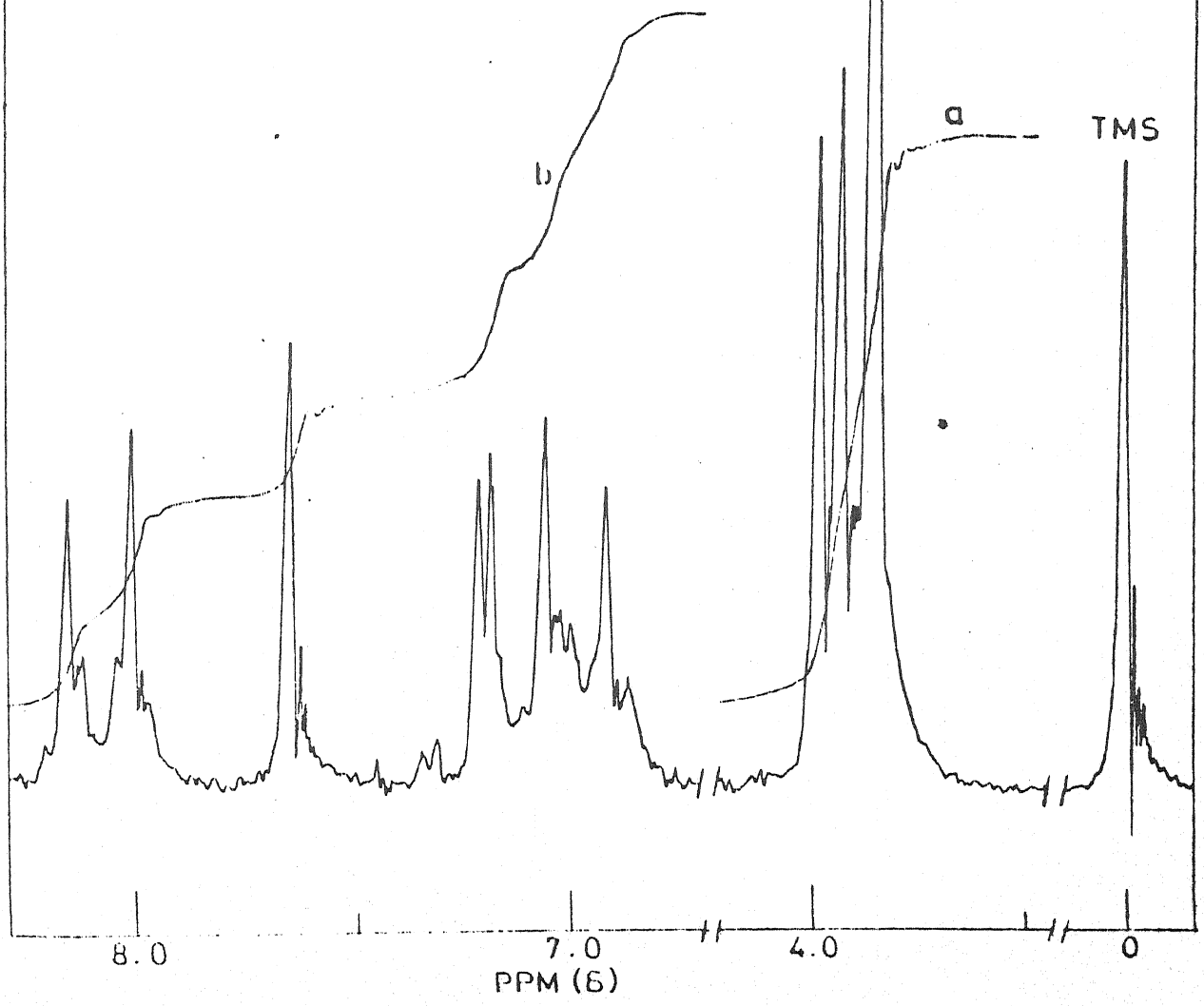


FIG. III. 5 NMR SPECTRUM OF 5h.

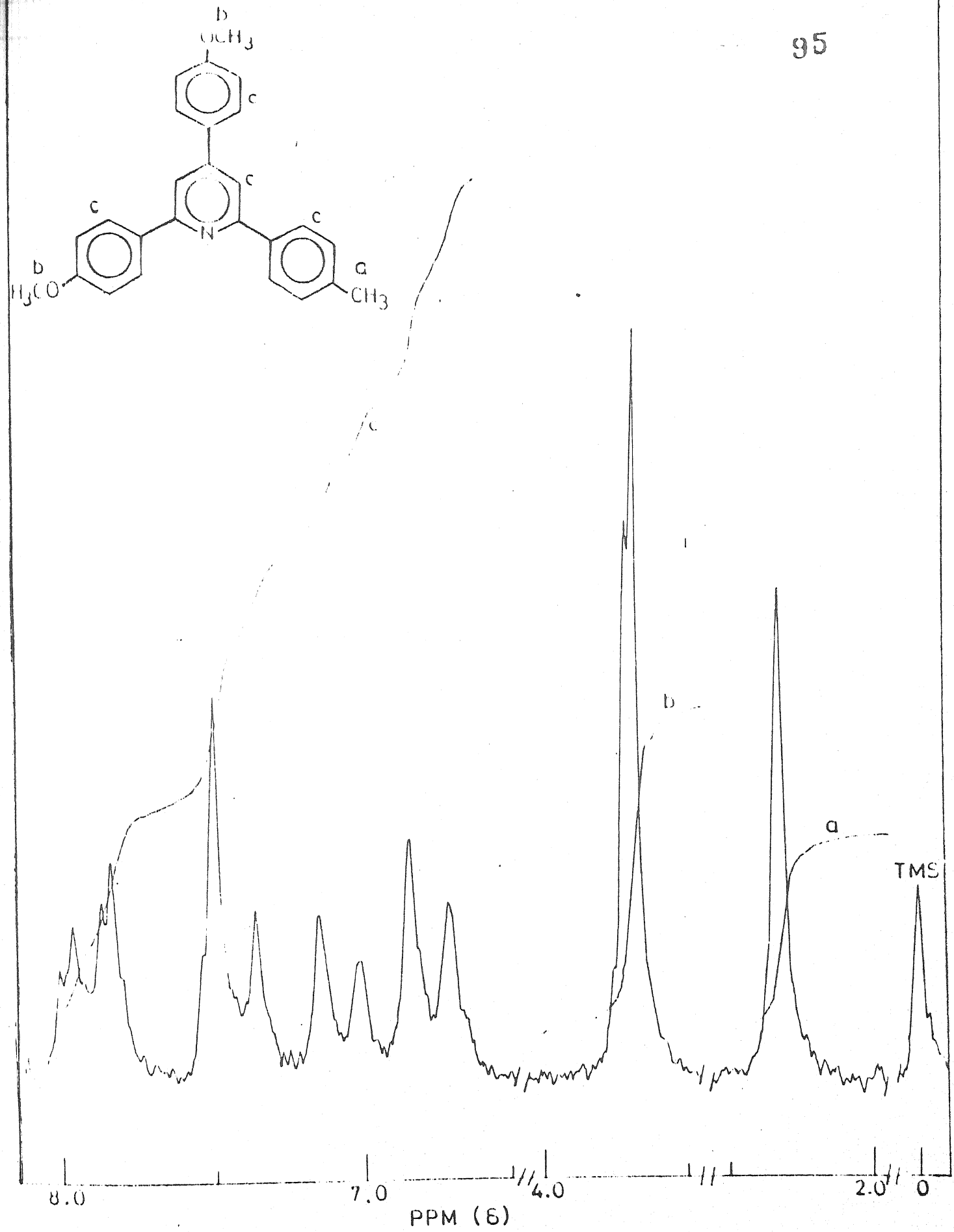


FIG. III.6 NMR SPECTRUM OF 51.

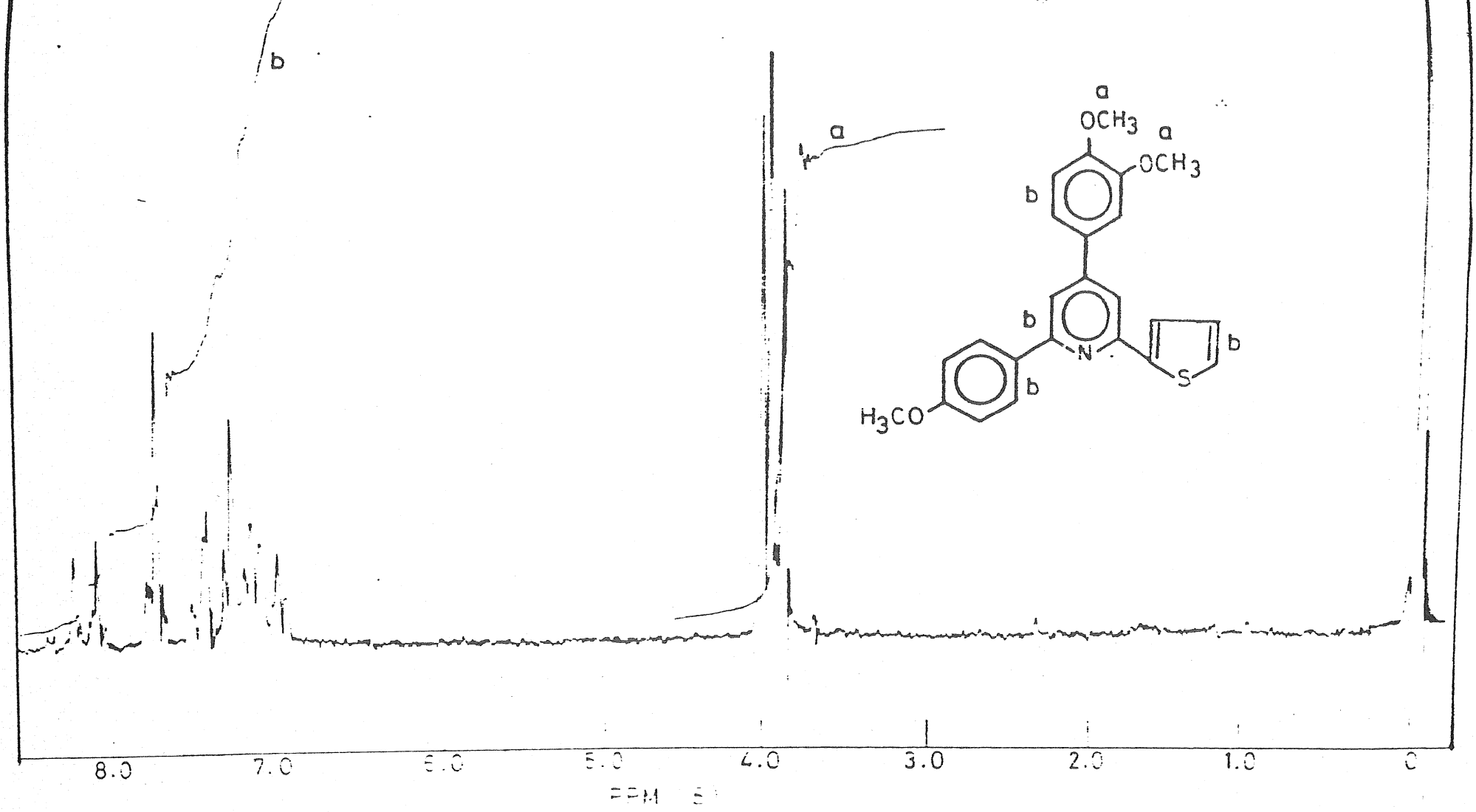


FIG III. 7 NMR SPECTRUM OF 5 o

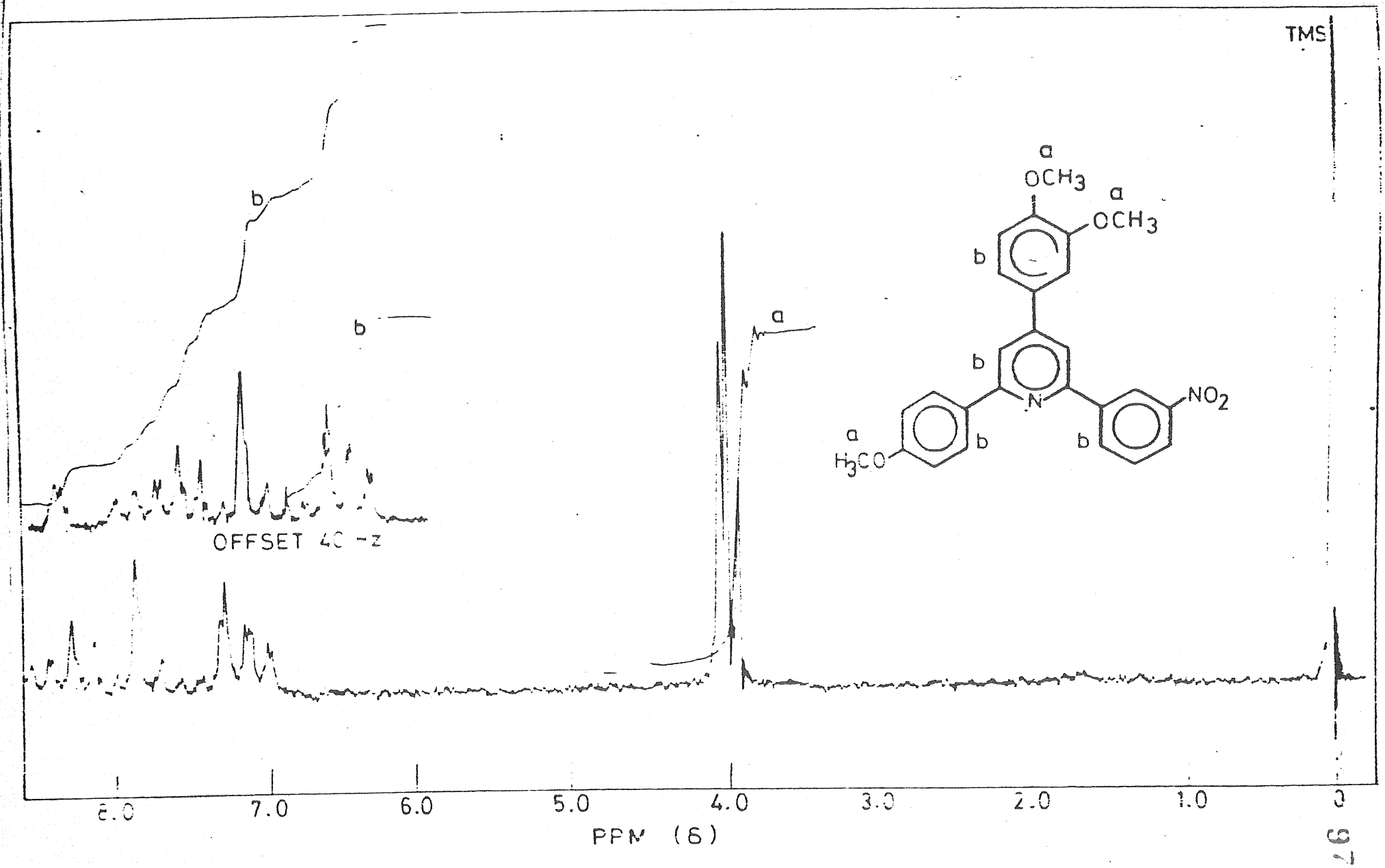


FIG. II.8 NMR SPECTRUM OF 5r.

was filtered and the clear filterate was treated with 10% aq.NaOH (15ml). The solution was stirred for 8 hrs, and then extracted several times with $CHCl_3$. The chloroform extract was dried with sodium sulphate and evaporated to give yellow oil which on cooling gave yellow solid. The yellow solid on crystallization with ethanol afforded reddish yellow crystals of 4-methoxyphenacylidenedimethyl sulfurane (2) in 80% yields which melted at 86-88°C (Lit.[20] m.p. 90°C).

IR Data (KBr) : 1500-1520Cm^{-1}

NMR($CDCl_3$) data(δ ppm) : 3.15(s,6H,di CH_3) : 3.70(s,3H,OCH_3) : 4.20(s,1H,$\bar{C}H$-$S^+<$) : 7.20-8.15(m,4H,Ar-H).

III.4.3. General Procedure for prepration of 2,4,6-triarylpyridines (5a-r) :

To a stirred mixture of 4-methoxyphenacyl sulfonium bromide (1) (3m mole) and ammonium acetate (3g) in glacial acetic acid (25ml), a solution of disubstituted benzylidene acetophenone (3a-r) (3m mole) dissolved in 20ml of glacial acetic acid was added dropwise by dropping funnel at the reflux temperature in an atmosphere of nitrogen. After complete addition of chalcome, the mixture was refluxed for 3-6 hrs and then left overnight at the room temperature. The mixture was then poured in ice cold water (50ml) which was constantly stirred. The solid mass precipitated, filtered and then washed with methanol. The product, on crystallization with an appropriate solvent, gave crystalline titled pyridines(5a-r) in 40-80% yields as depicted in table III.1.

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TABLE III.1. PHYSICAL PROPERTIES OF 2,4,6-TRIARYLPYRIDINES (5a-r)

Compound	X	Y	Yield %	M.P. °C	Lit.[20] M.P. °C	Recrystn. Solvent	Anal.data found/(Calcd.) C%	H%	N%
1	2	3	4	5	6	7	8	9	10
5a	4-Cl	4-OCH_3	64	143	144-45	A	74.69 (74.71)	4.95 (4.98)	3.46 (3.48)
b	4-Cl	4-Cl	72	196	195	A	70.91 (70.93)	4.20 (4.18)	3.45 (3.44)
c	4-OCH_3	4-OCH_3	56	124	126-27	A	78.55 (78.55)	5.77 (5.79)	3.54 (3.52)
d	4-Cl	4-$N(CH_3)_2$	62	127-29	128-30	A	75.28 (75.27)	5.56 (5.54)	6.72 (6.75)
e	4-Cl	3,4-$(OCH_3)_2$	59	119-21	118-20	A	72.32 (72.30)	5.06 (5.09)	3.21 (3.24)
f	4-OCH_3	4-Cl	76	124-28	125-30	A	74.70 (74.71)	4.96 (4.98)	3.46 (3.48)
g	4-OCH_3	4-$N(CH_3)_2$	73	111-13	110-12	B	79.00 (79.02)	6.36 (6.34)	6.80 (6.82)
h	4-OCH_3	3,4-$(OCH_3)_2$	52	81-83	80-82	B	75.84 (75.87)	5.86 (5.85)	3.28 (3.27)
i	4-OCH_3	3,4-CH_2O_2	59	124-26	125-26	B	75.89 (75.91)	5.08 (5.10)	3.38 (3.40)

CONTD. Table III.1.

1	2	3	4	5	6	7	8	9	10
j	4-Cl	3,4-CH_2O_2	53	134-39	135-40	B	72.16 (72.20)	4.31 (4.33)	3.38 (3.36)
k	4-CH_3	3,4-CH_2O_2	82	86	85	C	78.95 (78.98)	5.30 (5.31)	3.52 (3.54)
l	4-CH_3	4-OCH_3	61	103-5	104-5	B	81.86 (81.88)	6.04 (6.03)	3.65 (3.67)
m	2-$C_{10}H_7$	C_6H_5	66	194	195	B	86.89 (86.91)	6.04 (6.07)	3.25 (3.27)
n	2-$C_{10}H_7$	4-CH_3	47	133-34	135-36	B	86.84 (86.87)	6.31 (6.33)	3.14 (3.16)
o	2-C_4H_3S	3,4-$(OCH_3)_2$	53	96-98	97-98	B	71.43 (71.46)	5.19 (5.21)	3.49 (3.47)
p	4-CH_3	3,4-$(OCH_3)_2$	63	110-16	112-15	B	78.84 (78.83)	6.07 (6.08)	3.40 (3.40)
q	4-C_6H_5	C_6H_5	71	97	98	B	86.72 (86.74)	6.01 (6.02)	3.35 (3.37)
r	3-NO_2	3,4-$(OCH_3)_2$	62	144-47	146-47	C	70.55 (70.58)	4.96 (4.97)	6.36 (6.37)

A = Chloroform; ethanol B = Pyridine methanol C = Pyridine methanol water.

TABLE III.2. IR DATA (KBr) Cm^{-1} 2,4,6-TRIARYLPYRIDINES(5a-r)

Compound	IR Data (KBr) Cm^{-1}			
	ν C-H	ν C=C	ν C=N	ϕ C-H
5a	3030	1600	1550	995
b	3040	1605	1545	998
c	3030	1610	1552	990
d	3020	1595	1530	1005
e	2948	1598	1520	1030
f	3030	1600	1540	1020
g	3000	1595	1510	1020
h	3015	1000	1540	1005
i	3000	1600	1545	1030
j	3010	1600	1540	1015
k	3000	1600	1545	1035
l	3015	1605	1540	1010
m	3010	1600	1490	1030
n	3010	1600	1515	1030
o	3020	1590	1530	1005
p	3030	1595	1540	998
q	3010	1600	1535	1005
r	3000	1600	1515	1025

ν = Stretching vibrations; ϕ = Out of plane deformation of hydrogen attached to aromatic nucleus.

TABLE III.3. NMR($CDCl_3$) DATA OF 2,4,6-TRIARYLPYRIDINES (5a-r)

Compound	δ(ppm)	No.of protons	Assignment to protons
5a	3.64-3.82, d	6H	$(OCH_3)_2$
	6.63-8.02, m	14H	Ar-H+PyH
b	3.74, s	3H	OCH_3
	6.65-8.03, m	14H	Ar-H+PyH
c	3.88, s	9H	$(OCH_3)_3$
	6.96-8.21, m	14H	Ar-H+PyH
d	3.70, s	3H	OCH_3
	3.10, s	6H	$N(CH_3)$
	6.80-8.05, m	14H	Ar-H+PyH
e	3.70, s	3H	OCH_3
	3.85, d	6H	$(OCH_3)_2$
	6.95-8.10, m	13H	Ar-H+PyH
f	3.75, s	6H	$(OCH_3)_2$
	6.85-8.05, m	14H	Ar-H+PyH
g	3.80, s	6H	$(OCH_3)_2$
	3.10, s	6H	$N(CH_3)_2$
	6.90-8.15, m	14H	Ar-H+PyH
h	3.82-4.06, m	12H	$(OCH_3)_4$
	6.88-8.19, m	13H	Ar-H+PyH
i	3.75, d	6H	$(OCH_3)_2$
	5.95, s	2H	O_2CH_2
	7.05-8.15, m	13H	Ar-H+PyH

CONTD. III.3.

1	2	3	4
j	3.78, s	3H	OCH_3
	6.05, s	2H	O_2CH_2
	6.88-8.20, m	13H	Ar-H+PyH
k	2.35, s	3H	CH_3
	3.72, s	3H	OCH_3
	5.98, s	2H	O_2CH_2
	7.15-8.10, m	13H	Ar-H+PyH
l	2.33, s	3H	CH_3
	3.64-3.78, d	6H	$(OCH_3)_2$
	6.60-8.08, m	14H	Ar-H+PyH
m	3.80, s	3H	OCH_3
	7.15-8.35, m	18H	Ar-H+PyH
n	3.65, s	3H	OCH_3
	2.38, s	3H	CH_3
	7.15-8.25, m	17H	Ar-H+PyH
o	3.70, s	3H	OCH_3
	3.85, d	6H	$(OCH_3)_2$
	7.10-8.20, m	12H	Ar-H+PyH
p	2.40, s	3H	CH_3
	3.85, d	6H	$(OCH_3)_2$
	3.70, s	3H	(OCH_3)
	7.00-8.15, m	13H	Ar-H+PyH

CONTD. Table III.3.

1	2	3	4
q	3.75, s	3H	OCH_3
	7.15-8.25, m	20H	Ar-H+PyH
r	3.70, s	3H	OCH_3
	3.88, d	6H	$(OCH_3)_2$
	6.88-8.15, m	13H	Ar-H+PyH

s = Singlet; d = Doublet; m = Multiplet

CHAPTER IV

CHAPTER-IV

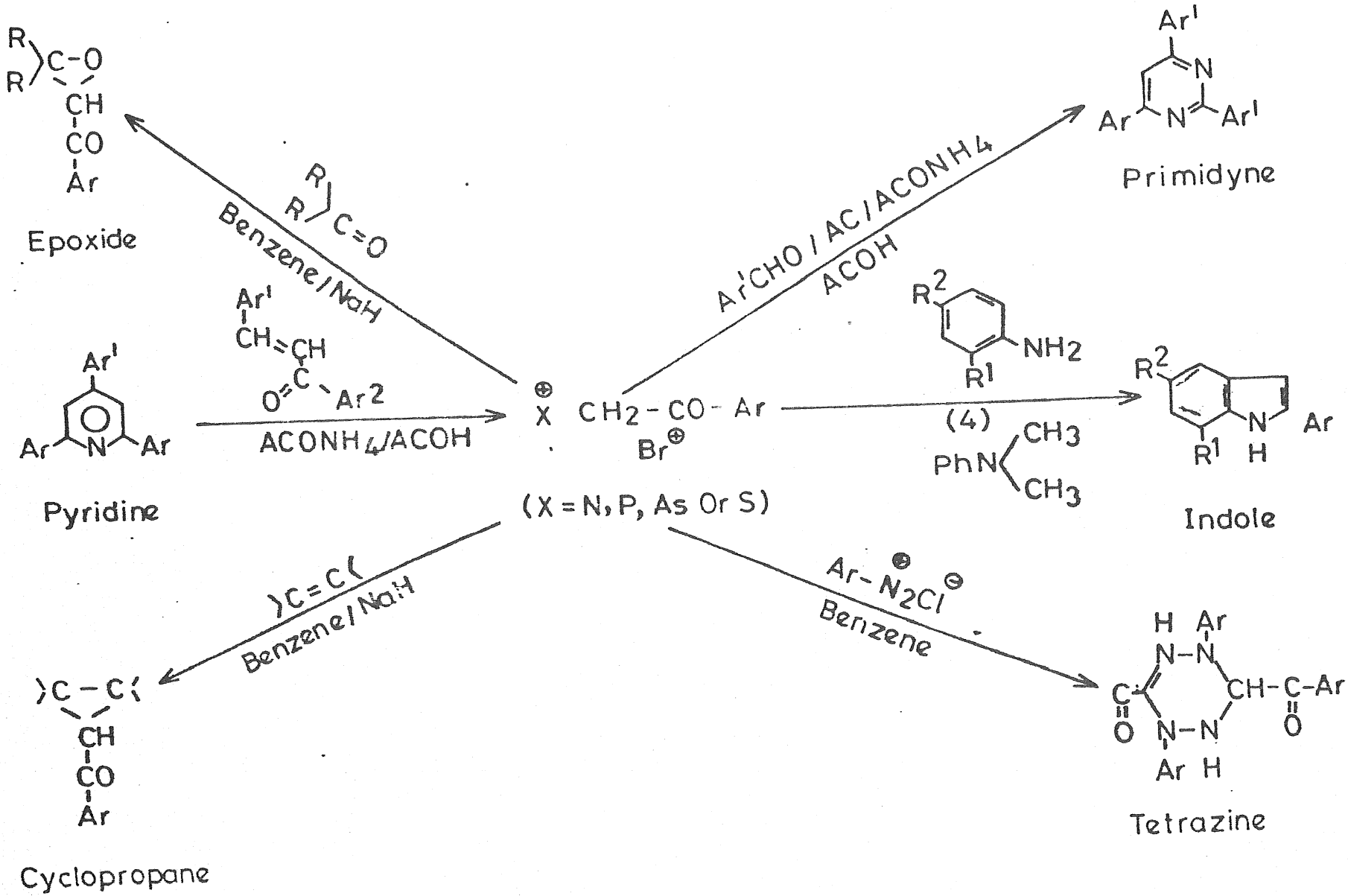
SYNTHESIS OF 2,4,6-TRISUBSTITUTED PHENYL PYRIMIDINES USING 4-NITROPHENACYL DIMETHYL SULFURANE AND 4-FLUOROPHENACYL DIMETHYL SULFURANE WITH AROMATIC ALDEHYDES.

IV.1. ABSTRACT :

4-Nitrophenacyl dimethyl sulfonium bromide and 4-fluorophenacyl dimethyl sulfonium bromide have been prepared by the reaction of dimethyl sulphide with 4-substituted phenacylbromide in benzene at reflux temperature in good yields. These sulfonium salts on treatment with NaOH gave corresponding 4-nitrophenacylidene dimethyl sulfurane and 4-fluorophanacylidene dimethyl sulfurane. Reaction of these sulfonium salts and sulfuranes with various aromatic aldehydes was carried out in presence of ammonium acetate and acetic acid at reflux temperature in an atmosphere of nitrogen gave 2,4,6-triaryl pyrimidine in 35-80% yields. Ammonium acetate in acetic acid was used as azacyclization agent. The structures of new pyrimidines were confirmed on the basis of IR and NMR spectra data.

IV.2. INTRODUCTION :

Pyridinium, phosphonium, arsonium and isoquinolinium have gained considerable importance in the synthesis of acyclic, cyclic and heterocyclic compounds[1-7](Scheme IV.1). Noteworthy in this regards are the synthesis of pyridines[1-2], Indoles[3],


Epoxide
Benzene/NaH
Ar'CHO / AC / ACONH4
ACOH
Primidyne
Pyridine
ACONH4/ACOH
(X = N, P, As Or S)
(4)
Indole
Benzene/NaH
Benzene
Cyclopropane
Tetrazine

Tetrazines[4], Cinnolines[5], Napthalenes[6], Epoxides[7], Cyclopropanes[7] and azaridines[7] and several other heterocycles. As reported earlier sulfonium salts and π-sulfuranes are better potential reagents than corresponding ylides of V group elements for the synthesis of heterocycles[8-15] Krohnke[16] first time reported in a single reaction involving condensation of phenacylpyridinium bromide with 4-nitrobenzaldehyde to yield 2,4-di-(4-nitrophenyl)-6-phenylpyrimidine. Detail experimental conditions were also not reported by Krohnke's et al[16]. Further more reaction of pyridinium ylides was not explored and duplicated with other aromatic aldehydes until recently. As in the several cases sulfonium and pyridinium ylides follows the same course of reaction[1-17]. Hence further extension of reaction leading to the pyrimidine nucleus seems to be pertinent. With a view the test of domain of applicability of sulfonium salts and π-sulfuranes. In the present chapter 4-nitrophenacyldimethyl-sulfonium bromide and 4-fluorophenacyldimethyl sulfonium bromide as well as their corresponding π-sulfuranes have been coupled with a wide range of aromatic aldehydes in presence of ammonium acetate and acetic acid at reflux temperature leading to aza ring closure to form pyrimidine necleus.

IV.3. RESULTS & DISCUSSION :

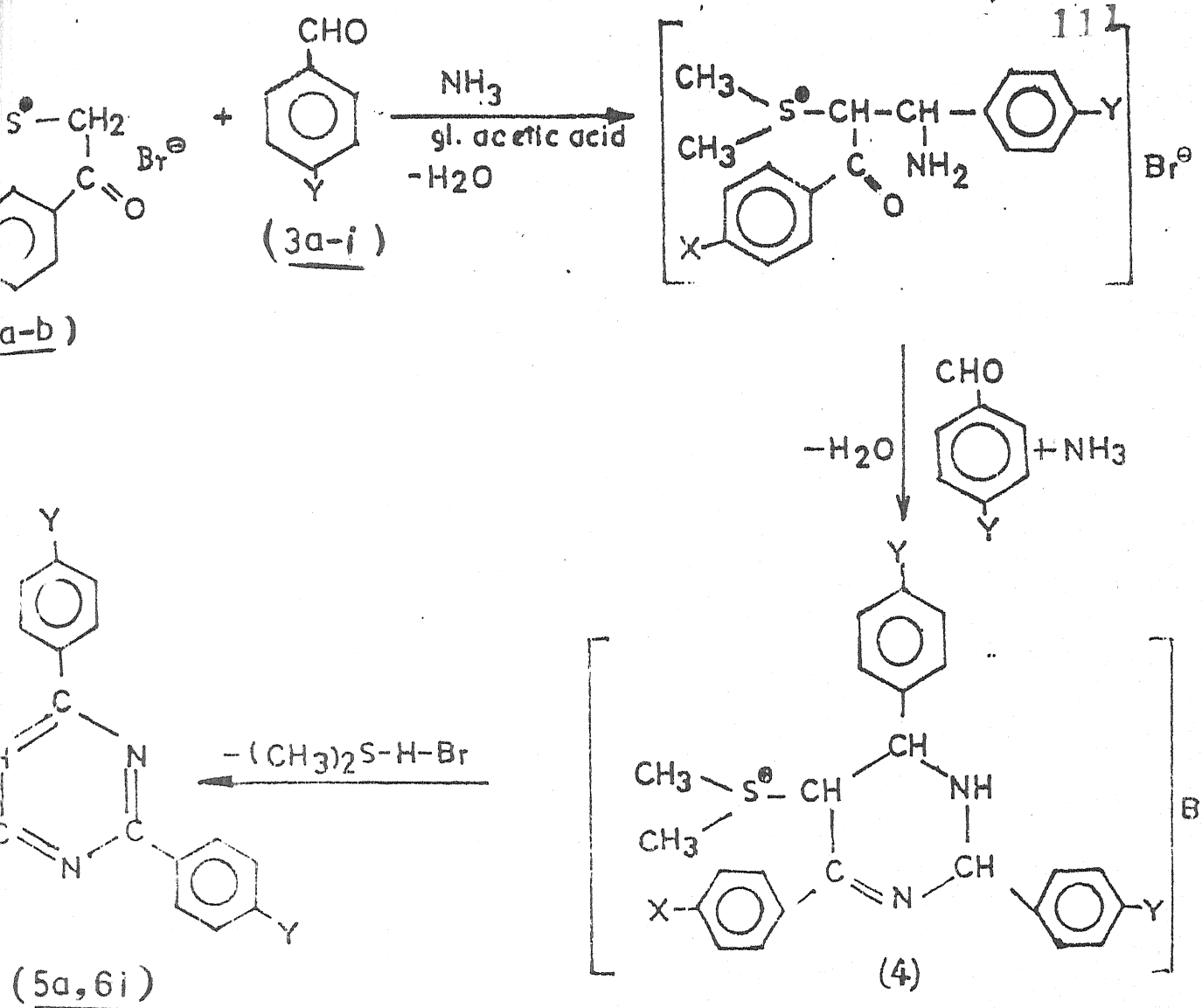
Reaction of dimethyl sulfide with 4-nitrophenacyl

bromide and 4-fluorophenacyl bromide in benzene at reflux temperature gave 4-nitrophenacyldimethyl sulfonium bromide(1a) 4-fluorophenacyl dimethyl sulfonium bromide (1b) in fair to good yields. The structure of sulfonium salts (1a-b) were confirmed by comperision of melting points of salts with those reported in the literature[15,17] and by spectral data. The IR spectra of salts (1a-b) showed a charecterstic absorption band due to C-O stretching vibrations in the region 1670-1690 Cm^{-1} for carbonyl group. The diagnostic absorption bands in the region 3300-3000 Cm^{-1} were observed due to C-H stretching vibrations of methylene group attached to sulfur atom[18,19].

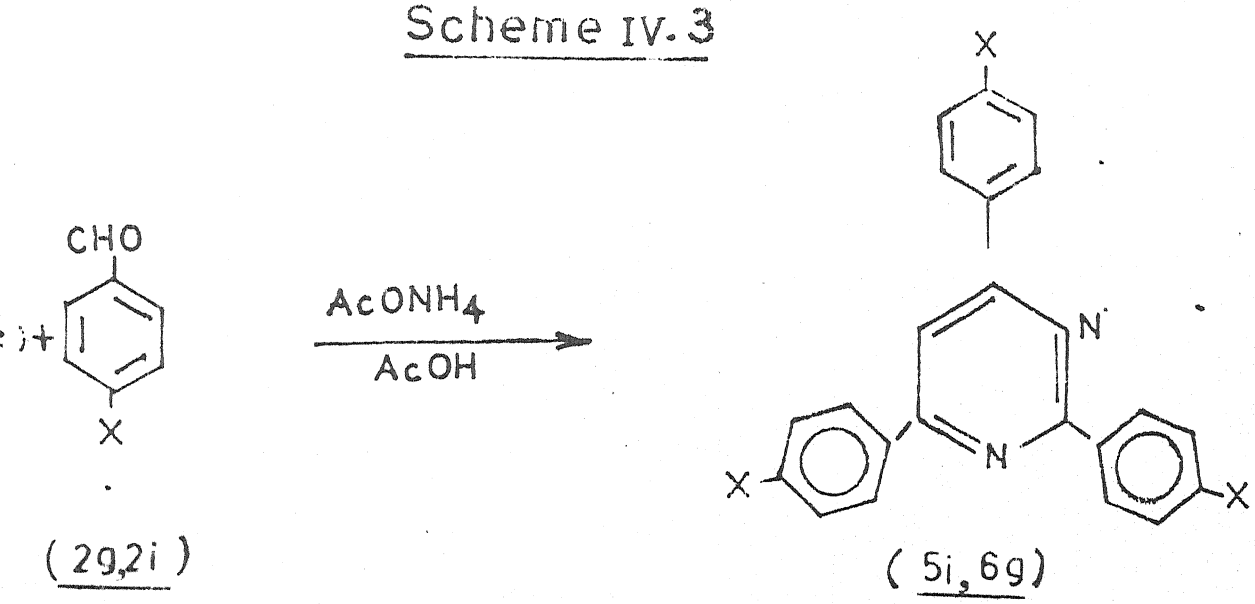
The treatment of these salts (1a-b) with aqueous sodium hydroxide/potassium carbonate gave 4-nitrobenzylidene dimethyl sulfurane (2a) and 4-fluorobenzylidene dimethyl sulfurane (2b) which could not be stored due to senstivity towards atmospheric components and lack of stabilizing factors. Hence they could not be used in subsequent reactions. The reaction was therefore carried out by generating the ylide intermediates (2a-b) in situ from the corresponding salts(1a-b).

Heating the mixture of sulfonium salts (1a-b) with substituted benzaldehyde (3a-i) in presence of ammonium acetate and glacial acetic acidmat reflux temperature gave 2,4,6-triaryl pyrimidines (5a-i, 6a-i) 35-80% yields (Scheme IV.2).

Scheme IV.2



Scheme IV.3



Further attempts were made to synthesize symmetrical pyrimidines having identical substituents at 2,4,6-positions. For this purpose 4-nitrophenacyldimethyl sulfonium bromide(1a) with 4-nitrobenzaldehyde and 4-fluorophenacyl dimethyl sulfonium bromide (1b) with 4-fluorobenzaldehyde were heated in a mixture of ammonium acetate and glacial acetic acid to give corresponding symmetrical pyrimidines viz.2,4,6-tri-(4-nitrophenyl) pyrimidines (5i) and (4-fluorophenyl) pyrimidines (6g) respectively in 65-60% yields(Scheme IV.3).

The reaction takes place through Mannich type reaction. The methylene group of salt (1a-b) with aromatic aldehydes (3a-i) in presence of ammonium acetate forms Mannich base-sulfonium salt (3) which inturn, undergoes condensation with another molecule of benzaldehyde in presence of ammonia to form sulfonium salt intermediate (4). The later, then undergoes elimination of dimethyl sulfonium hydrobromide to form 2,4,6-triaryl pyrimidines (5a-i,6a-i).

A number of 2,4,6-triaryl pyrimidines (5a-i) and (6a-i) synthesized by the above route are new and listed in table IV.1. All the pyrimidines gave satisfactory elemental and spectral analysis. The IR spectral data (Table IV.2) showed a charecterstic absorption bands in the region $3100Cm^{-1}$-$3000Cm^{-1}$ which were assigned due to C-H stretching mode of pyrimidine ring. The bands in the region $1600-1500Cm^{-1}$ were due to

interaction between C=C and C=N vibrations of the ring. The NMR spectra (table IV.3) of pyrimidines showed pyrimidal proton (C_5-H) in the range δ 6.40-6.80 and aromatic protons at δ 6.60-8.40.

IV.4. EXPERIMENTAL :

IV.4.1. Starting Material :

All the reagents were obtained from commercial source (E. Merck, BDH, SISCO etc.). Starting materials viz.4-nitrophenacyl bromide and 4-fluorophenacyl bromide were prepared according to the procedure reported in literature[20].

IV.4.2. Preparation of 4-nitrophenacyl dimethyl sulfonium bromide(1a):

A solution of 100m mole of 4-nitrophenacyl bromide and 100m mole of dimethyl sulfide in 100ml of anhydrous acetone was stirred for 6-8 hrs.at room temperature in an atmosphere of nitrogen gave solid mass which was filtered, washed twice with acetone and crystallized from benzene pet.ether. The compound which was obtained has yellow coloured micro crystals m.p.150-152°C (Lit.[15] m.p. 152-154°C).

IR data (KBr): 1680Cm^{-1}(νC=O) 1570,1330Cm^{-1}(ν C-NO_2)

NMR($CDCl_3$): δ 3.30(s,6H,di CH_3): δ5.50(s,2H, $\underline{CH_2}$):

δ 7.30-7.90(m,4H,Ar-H)

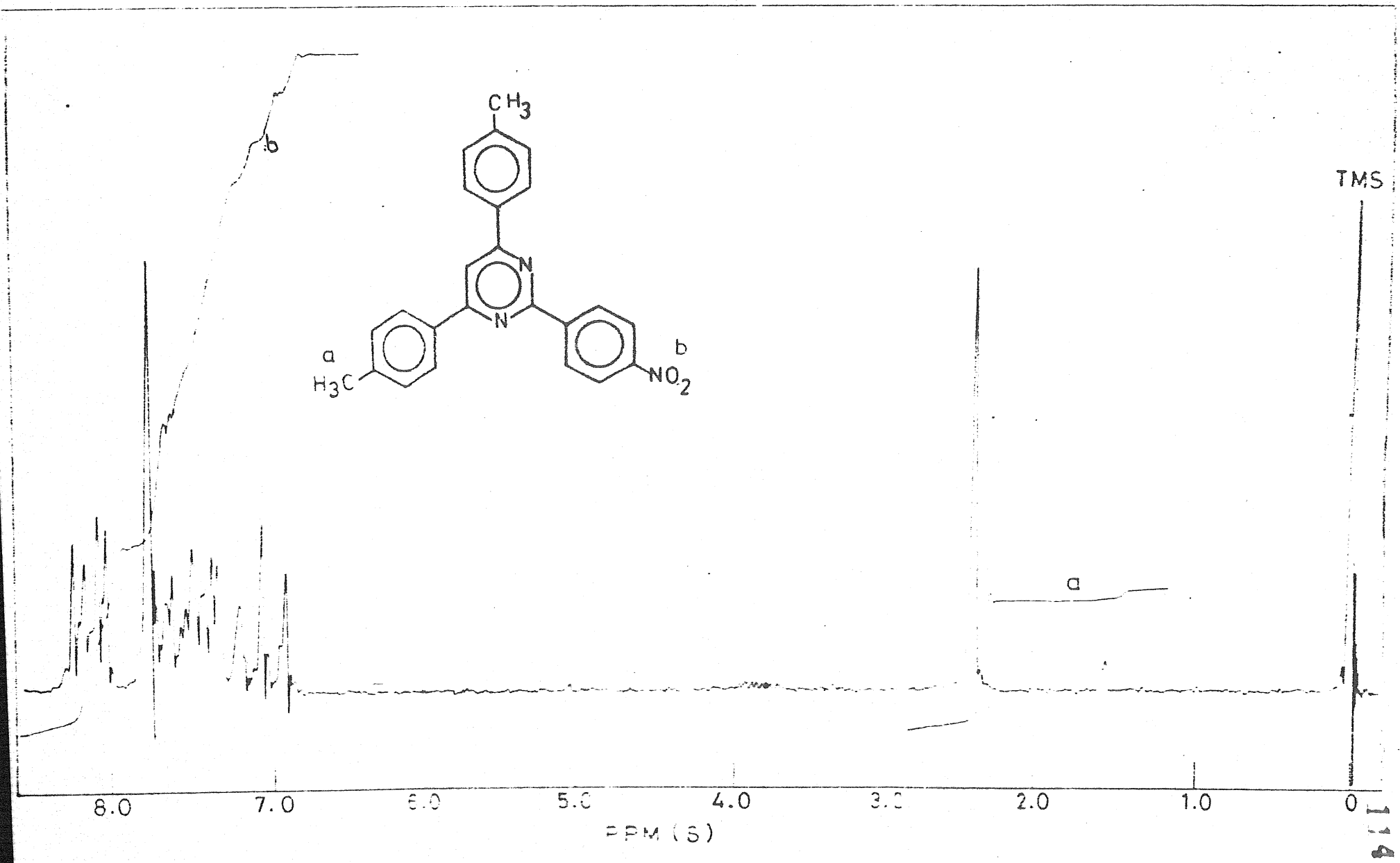


FIG. IV. 1 NMR SPECTRUM OF 5b.

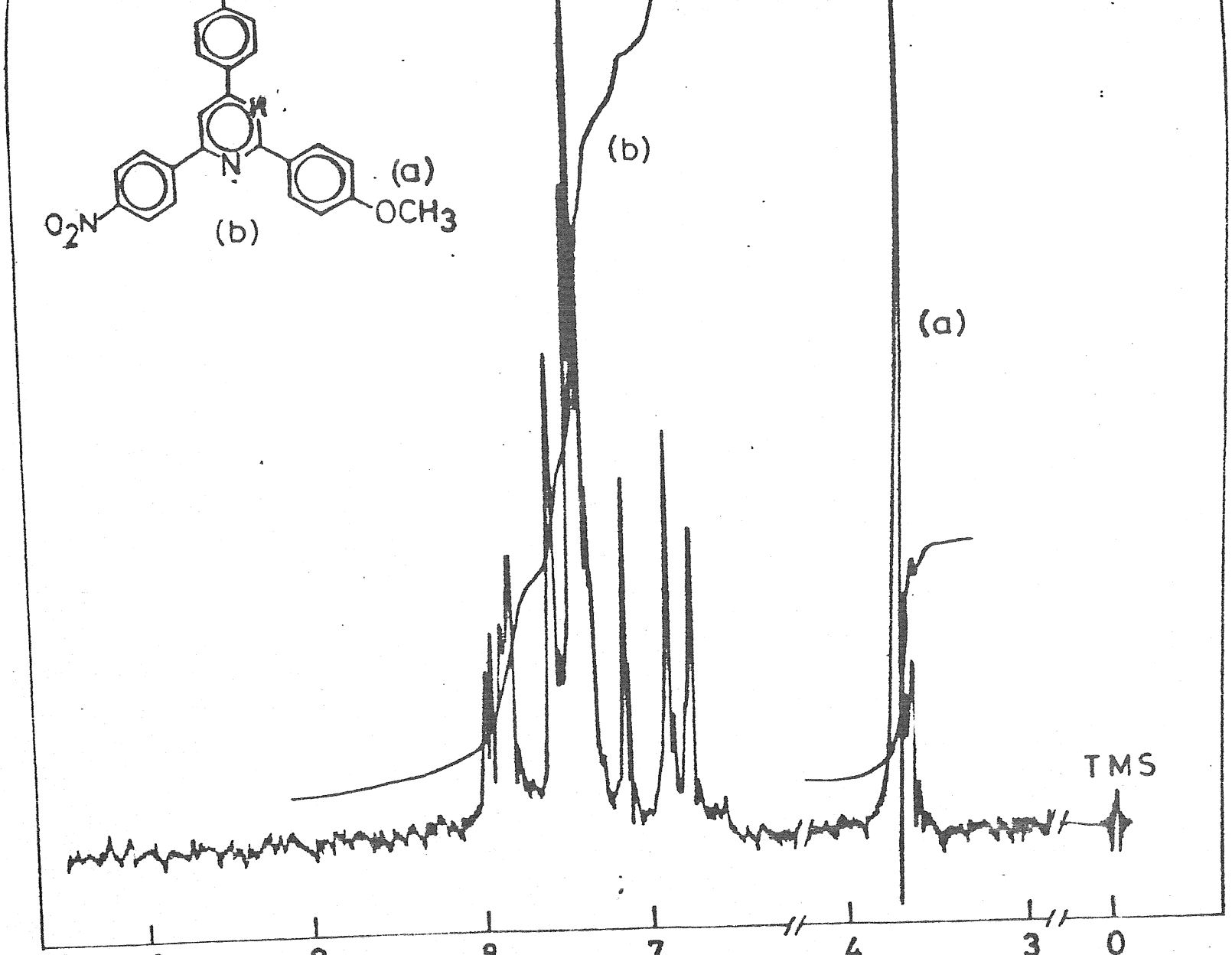


FIG. IV.2 NMR SPECTRUM OF COMPOUND (5d)

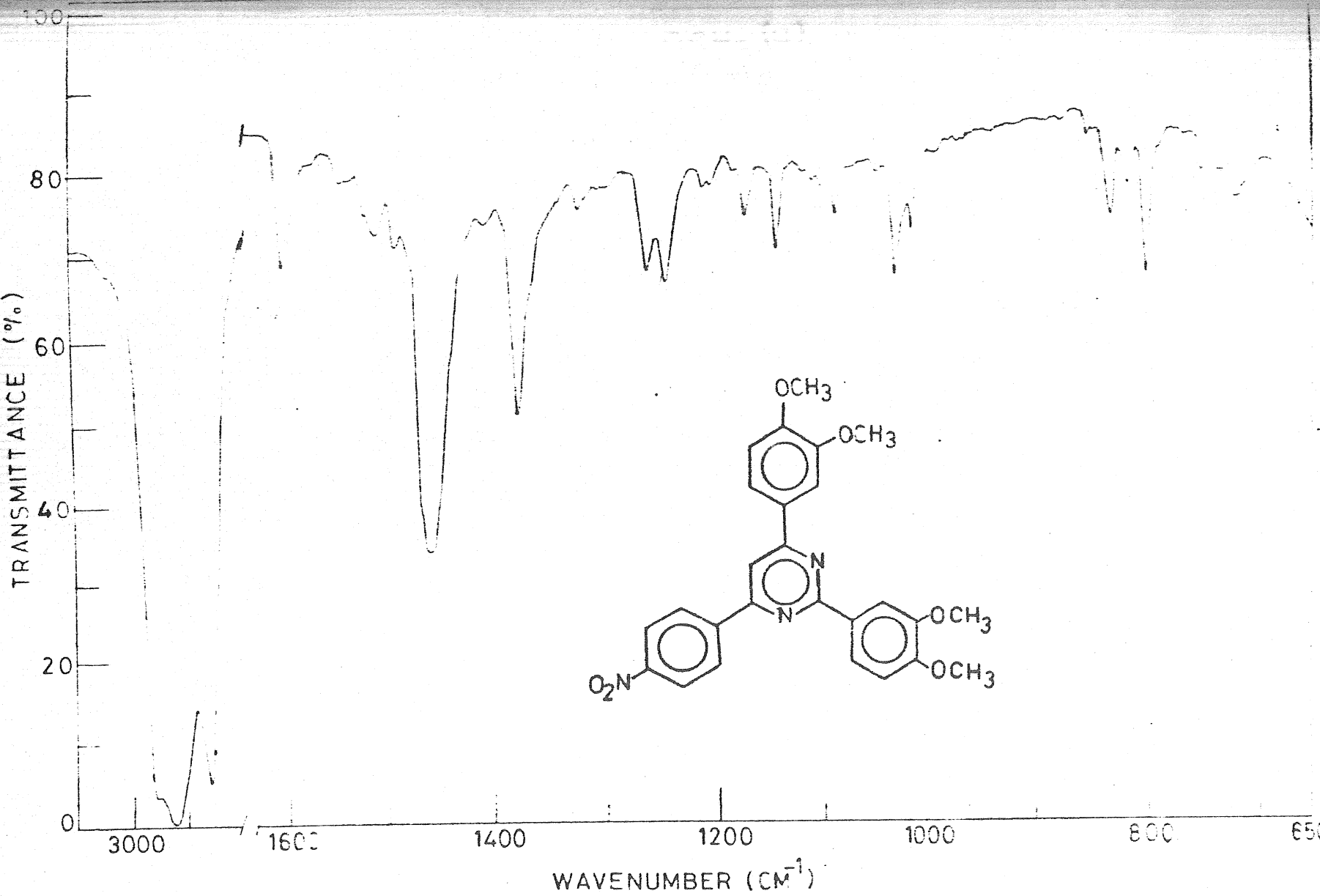


FIG.IV.3 IR SPECTRUM OF 5h

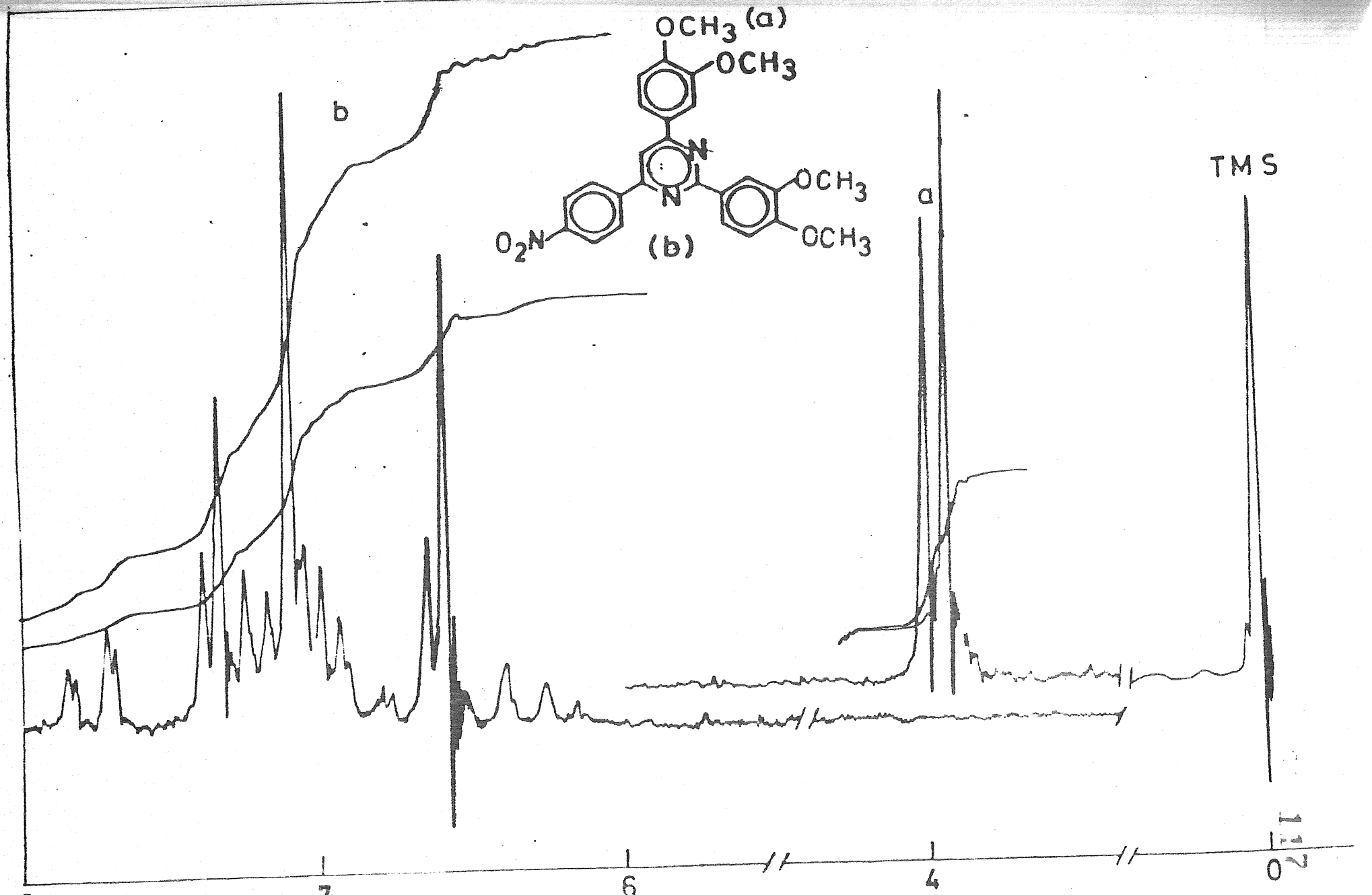


FIG IV. 4 ... SPECT... OF COMPOUND (5b)

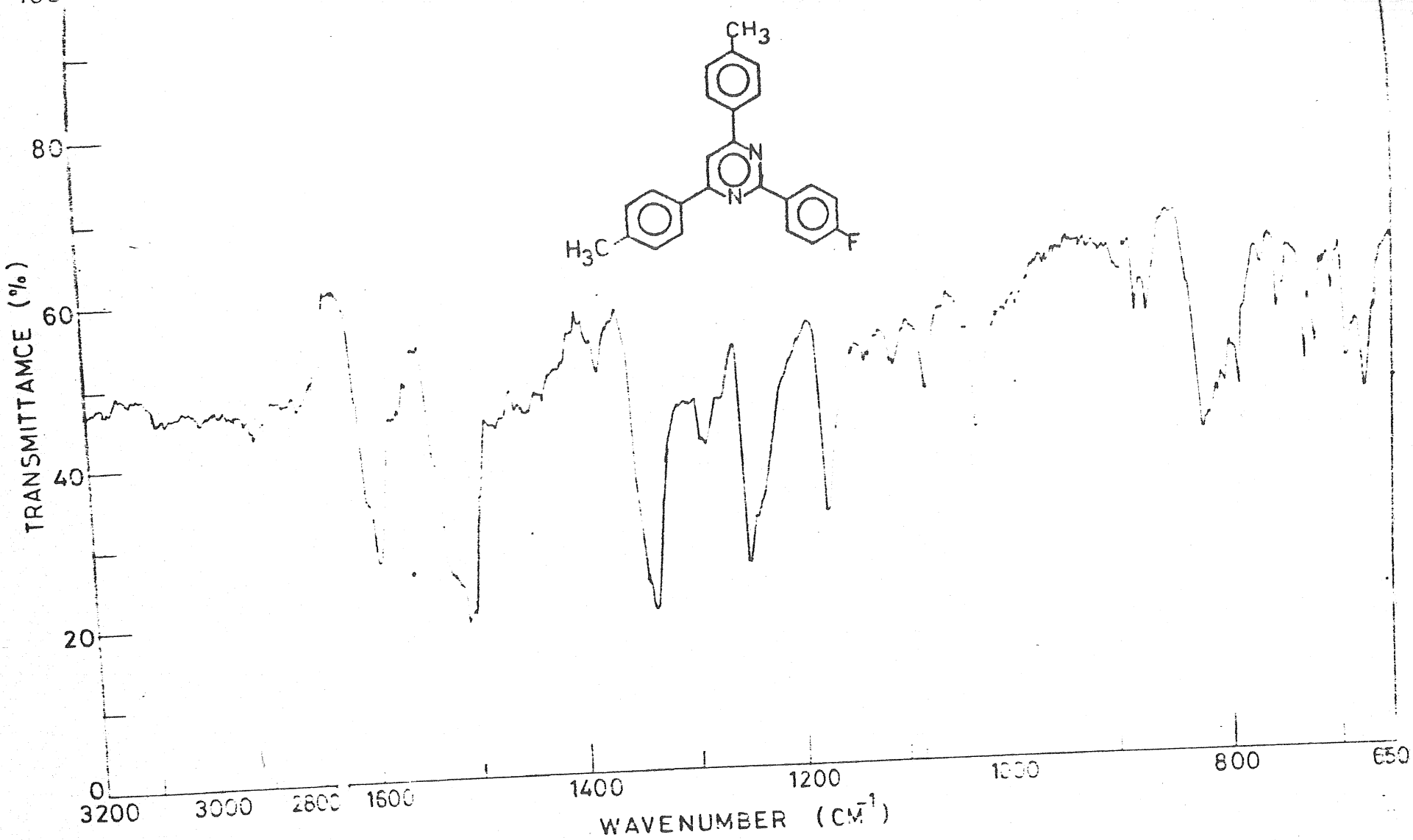


FIG. IV.5 IR SPECTRUM OF 6b.

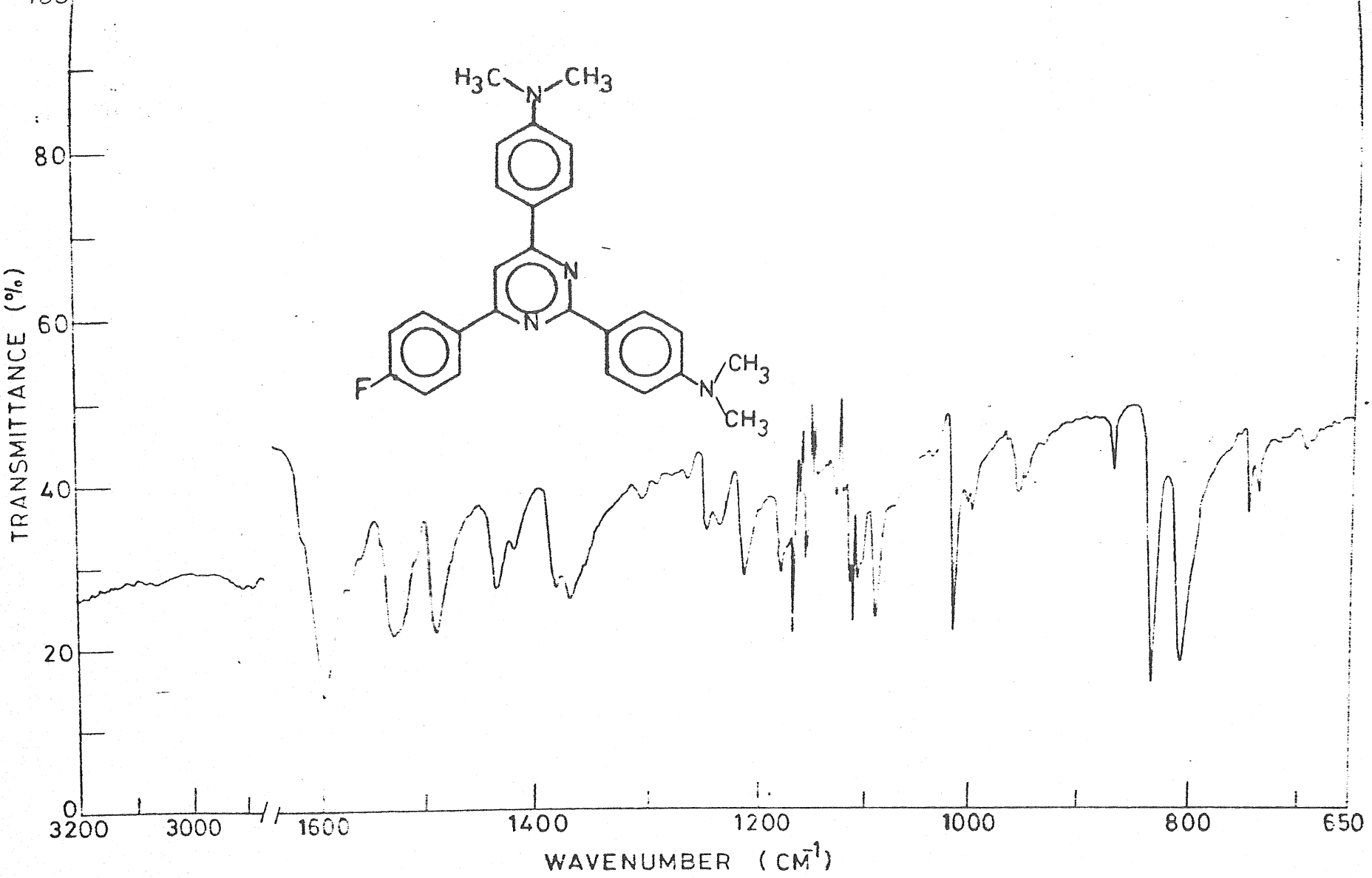


FIG. IV.6 IR SPECTRUM OF 6c.

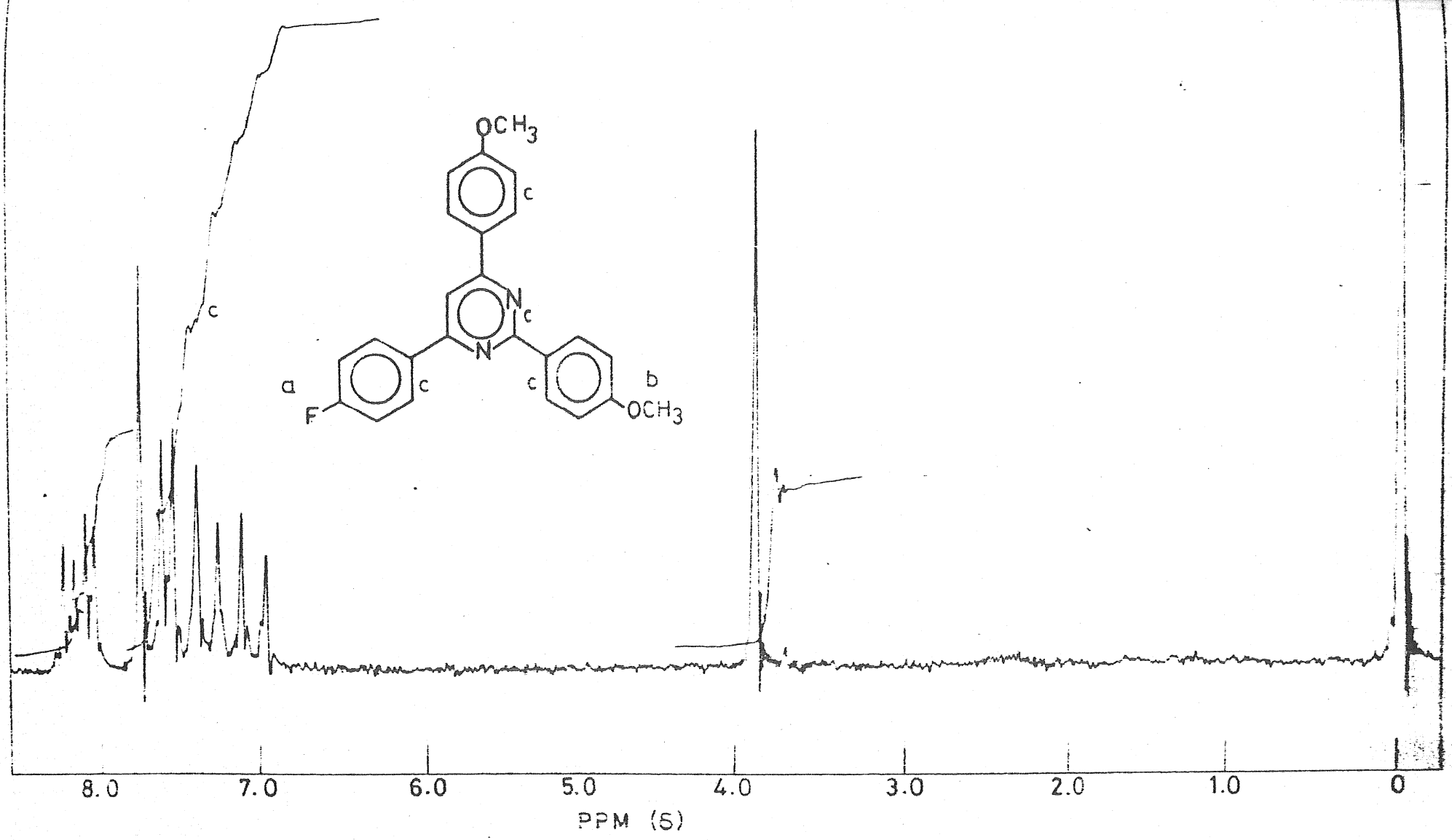


FIG. IV. 7 NMR SPECTRUM OF 6d.

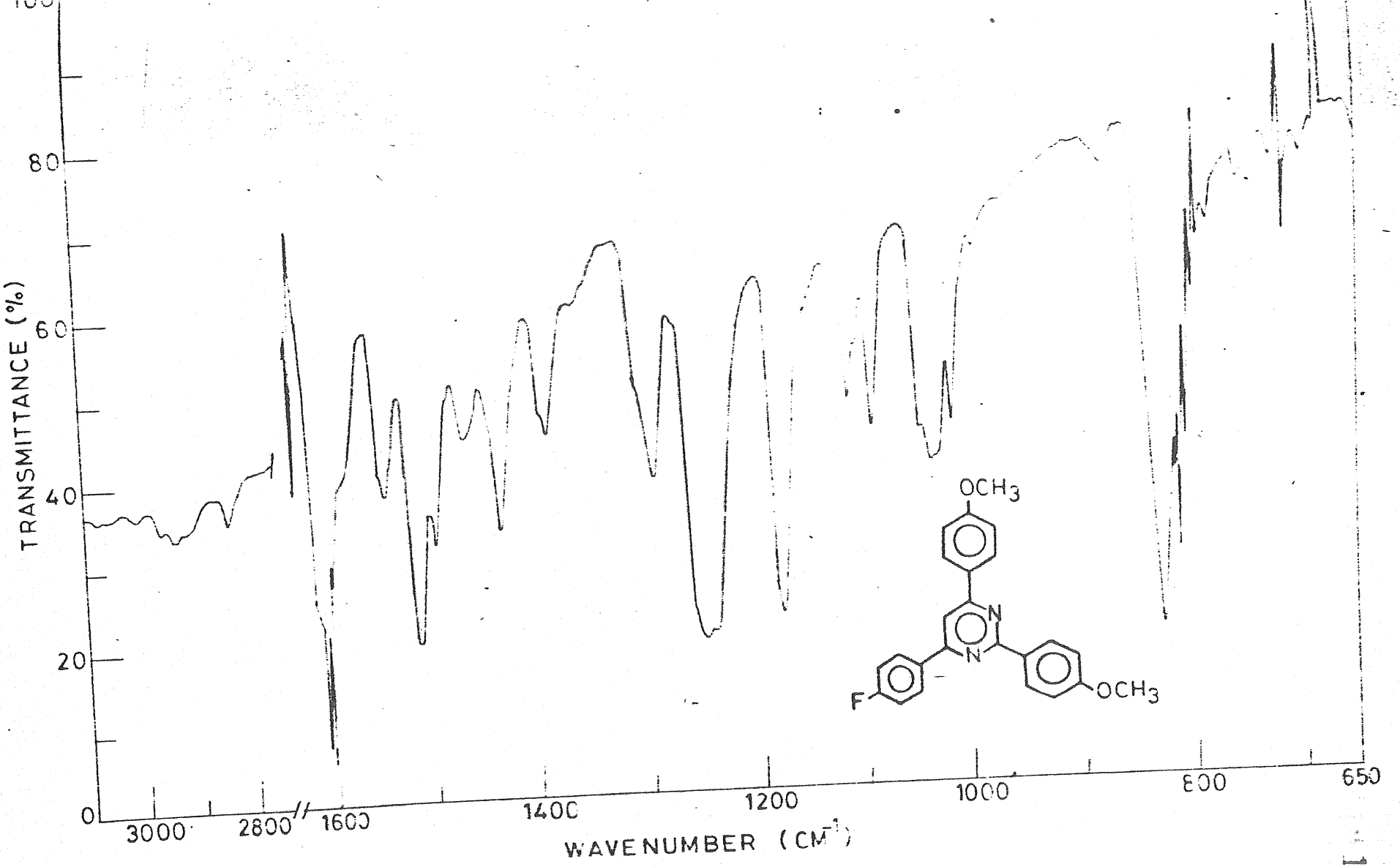


FIG. IV.8 IR SPECTRUM OF 6d.

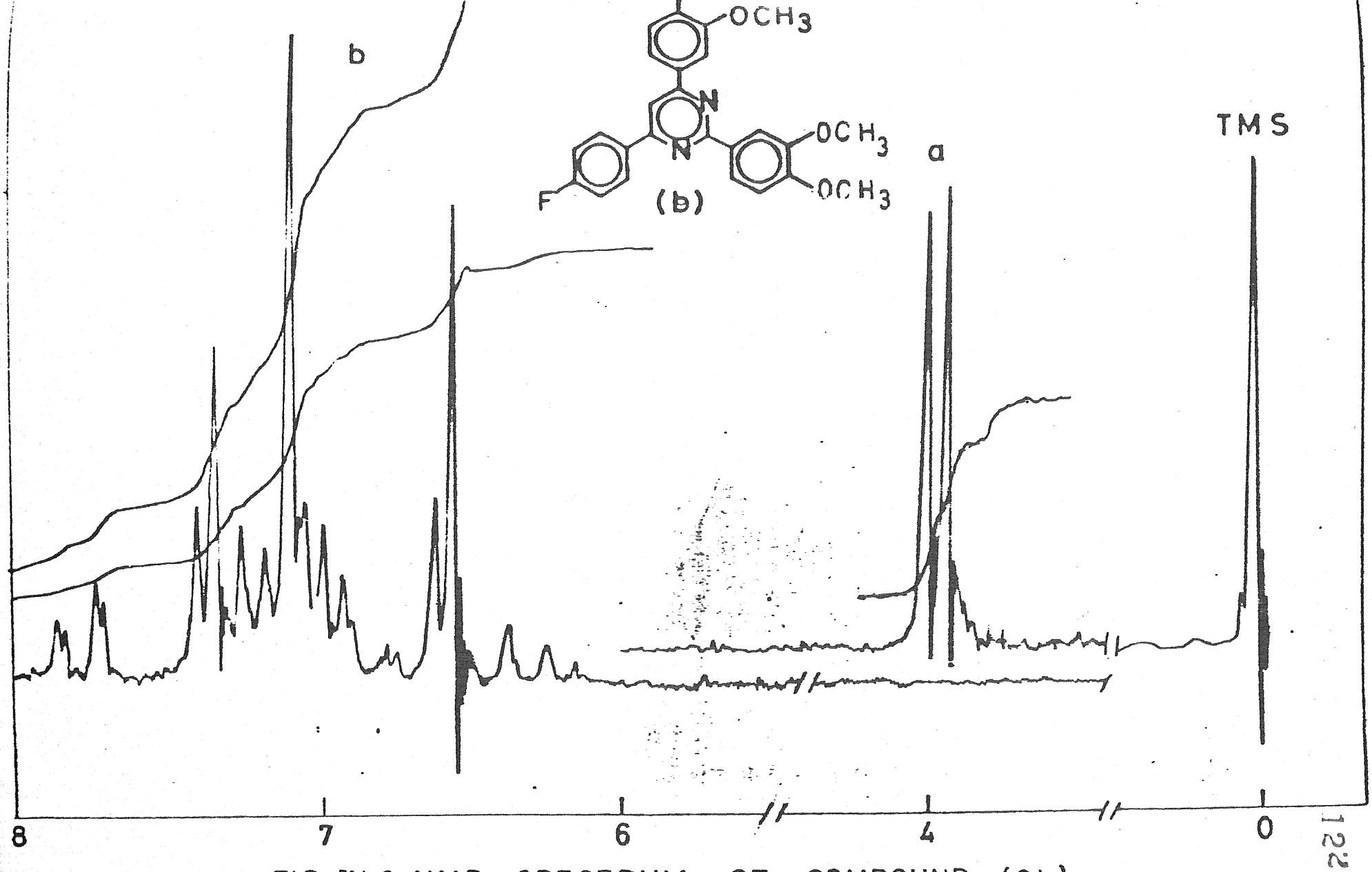


FIG. IV-9 NMR SPECTRUM OF COMPOUND (6h)

IV.4.3. Prepration of 4-nitrophenacylidenedimethyl sulfurane (2a) :

4-Nitrophenycylidenedimethyl sulfonium bromide(1a) (50m mole) was dissolved in water (30ml). The coloured suspension was filtered and the clear filterate was treated with 10% aq.NaOH (15ml). The solution was stirred for 8 hrs under nitrogen atmosphere and then extracted several time with $CHCl_3$. The chloroform extract was dried with sodium sulphate and evaporated to give yellow oil which on cooling gave yellow solid. The yellow solid on crystallization with ethanol afforded reddish yellow crystal of 4-nitrophenacylidene dimethyl sulfurane(2a) in 85% yield. Which melted at 64-66°C (Lit.[15] m.p.66-68°C).

IR data (KBr)max.: 3020Cm^{-1} (νC-H): 1670Cm^{-1} (νC=O)

NMR($CDCl_3$) (δ ppm): 3.20(s,6H, di CH_3) 5.50(s,2H, CH_2): 7.35-8.90(m, 4H, ArH)

IV.4.4. Prepration of 4-fluorophenacyl bromide (1b):

Stirring a mixture of 4-fluorophenacyl bromide(0.1 mole) and dimethyl sulfide (30ml) for 8 hrs gave white solid mass. The solid mass was filtered, washed twice with ether and recrystallized from alcohal as white colourless microcrystals m.p.140-142°C (Lit.[17] m.p. 142-144°C).

IR data (KBr) max: 3100 (ArH), 1675Cm^{-1} (νC=O)

NMR($CDCl_3$) (δ ppm): 3.26(s,6H,di CH_3): 5.45(s,2H,$\underline{CH}_2$): 7.25-7.85 (m,4H,ArH).

IV.4.5. Prepration of 4-fluorophenacylidene dimethyl sulfurane (2b):

4-Fluorophenacyl dimethyl sulfonium bromide(1b) (50m mole) was dissolved in water (30ml). The coloured suspension was filtered with 10% aq.NaOH (15ml). The solution was stirred for 8 hrs and then extracted several times with $CHCl_3$. The chloroform extract was dried with sodium sulphate and evaporated to give light yellow oil which on cooling gave light yellow solid. The light yellow solid on crystallization with ethanol afforded light reddish yellow crystals of 4-fluorophenacylidene dimethyl sulfurane (2) in 85% yields which melted at 68-69°C(Lit.[17] m.p. 69-70°C).

IR data (KBr) max: 2980 (Ar-H); 1520 Cm^{-1} (νC=O)

NMR ($CDCl_3$) (δ ppm): 3.16(s,6H,di CH_3): 4.31(s,1H,$\underline{CH_2}$): 7.28-7.97(m,4H,ArH)

IV.4.6. Prepration of 2,4,6-triaryl pyrimidines (5a-i,6a-i):

General Procedure :

A mixture of 3m mole 4-substituted phenacyl dimethylsulfonium bromide (1a-b) and 6m mole of aromatic aldehyde (2) and 3gm of ammonium acetate in 50ml of glacial acetic acid was stirred at room temperature. The mixture was then poured in ice cold water (50ml) which was constantly stirred. The solid mass was precipitated, filtered and washed

twice with water and then with methanol and dried. The product, on crystallization with appropriate solvents, gave crystalline 2,4,6-triarylpyrimidine(5a-i) & (6a-i) in good yields as computed in table IV.1.

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TABLE IV.1. PHYSICAL PROPERTIES OF 2,4,6-TRIARYLPYRIDINES (5a-i, 6a-i)

Compound	X	Y	Yield %	M.P. °C	Recrystn. Solvent	Analysis found/(Calcd.) C%	H%	N%
1	2	3	4	5	6	7	8	9
5a	4-NO_2	H	45	110-12	A	74.02 (74.05)	4.35 (4.37)	12.20 (12.24)
b	4-NO_2	4-CH_3	40	96-98	B	75.61 (75.59)	4.93 (4.98)	11.04 (11.02)
c	4-NO_2	4-$N(CH_3)_2$	45	120-22	A	71.03 (71.07)	5.67 (5.69)	15.99 (15.95)
d	4-NO_2	4-OCH_3	60	128-30	C	69.70 (69.73)	4.62 (4.60)	10.14 (10.16)
e	4-NO_2	4-Cl	65	78-80	A	62.54 (62.56)	3.04 (3.08)	10.07 (10.05)
f	4-NO_2	4-Br	55	86-88	B	55.76 (55.81)	2.71 (2.75)	8.82 (8.88)
g	4-NO_2	4-F	65	110-12	C	67.80 (67.87)	3.36 (3.34)	9.27 (9.26)
h	4-NO_2	3,4-di(OCH_3)	48	122-24	A	70.40 (70.42)	5.68 (5.64)	9.42 (9.48)
i	4-NO_2	4-NO_2	80	132-34	C	59.55 (59.59)	2.90 (2.93)	15.82 (15.80)

CONTD. Table IV.1.

1	2	3	4	5	6	7	8	9
6a	4-F	H	48	98-10	D	80.92 (80.98)	4.62 (4.60)	11.62 (11.64)
b	4-F	4-CH_3	45	112-14	B	81.34 (81.36)	5.37 (5.37)	7.92 (7.90)
c	4-F	4-$N(CH_3)_2$	41	124-26	C	75.70 (75.72)	6.06 (6.07)	13.52 (13.59)
d	4-F	4-OCH_3	42	130-32	A	78.42 (78.47)	5.15 (5.17)	7.64 (7.62)
e	4-F	4-Cl	50	76-78	C	66.80 (66.84)	3.26 (3.29)	7.05 (7.08)
f	4-F	4-Br	55	88-90	A	57.80 (57.85)	2.67 (2.69)	5.75 (5.79)
g	4-F	4-F	60	108-10	B	72.90 (72.93)	3.52 (3.59)	7.70 (7.73)
h	4-F	3,4-di(OCH_3)	50	124-26	A	69.94 (69.99)	5.13 (5.15)	6.24 (6.28)
i	4-F	4-NO_2	45	128-30	C	63.42 (63.46)	3.10 (3.12)	13.42 (13.46)

A = CH_3OH : $CHCl_3$ B = C_6H_6 : $CHCl_3$ C = C_5H_5N : CH_3OH

TABLE IV.2. IR DATA (KBr) Cm^{-1} 2,4,6-TRIARYLPYRIMIDINES (5a-i, 6a-i)

Compound	IR Data (KBr) Cm^{-1}				
	ν C-H	ν C=C	ν C=N	ϕ C-H	ν C-NO_2
5a	3110	1605	1510	995	1555, 1325
b	3085	1615	1525	990	1575, 1330
c	3105	1605	1510	995	1580, 1335
d	3115	1610	1520	992	1585, 1335
e	3060	1608	1505	990	1580, 1340
f	3110	1595	1500	1000	1575, 1320
g	3080	1598	1505	1005	1570, 1325
h	3108	1605	1510	1000	1580, 1330
i	3070	1610	1510	1005	1575, 1320
6a	3090	1600	1505	998	1580, 1335
b	3105	1605	1510	1005	1580, 1335
c	3100	1615	1500	992	1560, 1330
d	3065	1598	1500	1000	1570, 1330
e	3080	1605	1510	1010	1580, 1335
f	3100	1615	1505	992	1580, 1320
g	3105	1614	1505	995	1560, 1340
h	3080	1600	1500	998	1575, 1330
i	3095	1608	1505	990	1560, 1320

ν = Stretching vibrations; ϕ = Out of plane deformation of hydrogen attached to aromatic nucleus.

TABLE IV.3. NMR ($CDCl_3$) DATA OF 2,4,6-TRIARYLPYRIMIDINES (5a-i, 6a-i)

Cpmpound	δ (ppm)	No.of protons	Assignment to protons
1	2	3	4
5a	6.65, s	1H	PyH (C_5-H)
	6.85-6.88, m	14H	Ar-H
b	6.65, s	1H	PyH (C_5-H)
	2.35, s	6H	di CH_3
	6.95-8.20, m	12H	Ar-H
c	6.65, s	1H	PyH (C_5-H)
	3.95, s	12H	di N-$(CH_3)_2$
	6.75-7.85, m	12H	Ar-H
d	6.66, s	1H	PyH (C_5-H)
	3.85, s	6H	di (OCH_3)
	6.95-8.35, m	12H	Ar-H
e	6.78, s	1H	PyH (C_5-H)
	7.0-8.25, m	12H	Ar-H
f	6.80, s	1H	PyH (C_5-H)
	6.95-8.20, m	12H	Ar-H
g	6.75, s	1H	PyH (C_5-H)
	7.10-8.35, m	12H	Ar-H
h	6.65, s	1H	PyH (C_5-H)
	3.95, d, ($J=6H_z$)	12H	di(3,4-di OCH_3)
	6.85-7.85, m	10H	Ar-H
i	6.75, s	1H	PyH (C_5-H)
	7.05-8.35, m	12H	Ar-H

CONTD. Table IV.3.

1	2	3	4
6a	6.60, s	1H	PyH (C_5-H)
	6.75-7.95, m	14H	Ar-H
b	6.65, s	1H	PyH (C_5-H)
	2.50, s	6H	di-CH_3
	6.85-8.15, m	12H	Ar-H
c	6.70, s	1H	PyH (C_5-H)
	2.95, s	12H	di N-$(CH_3)_2$
	6.85-8.15, m	12H	Ar-H
d	6.60, s	1H	PyH (C_5-H)
	3.95, s	6H	di (OCH_3)
	6.90-8.35, m	12H	Ar-H
e	6.75, s	1H	PyH (C_5-H)
	7.05-8.35, m	12H	Ar-H
f	6.80, s	1H	PyH (C_5-H)
	7.15-8.45, m	12H	Ar-H
g	6.85, s	1H	PyH (C_5-H)
	7.10-8.35, m	12H	Ar-H
h	6.60, s	1H	PyH (C_5-H)
	3.85,d(J=6H_z)	12H	di(3,4-di OCH_3)
	6.95-8.28, m	10H	Ar-H
i	6.70, s	1H	PyH (C_5-H)
	7.10-8.30, m	12H	Ar-H

s = singlet m = multiplet d= doublet

CHAPTER V

CHAPTER-V

STUDIES ON METALLATION OF p - SUBSTITUTED PHENACYLIDENEDIMETHYL SULFURANES : Hg(II),Cd(II),Co(II) AND Ni(II) COMPLEXES OF AMBIDENTATE SULFURANES

V.1. ABSTRACT :

The synthesis of Hg(II), Cd(II),Co(II) and Ni(II) halides complexes with p-substituted dimethylsulfonium ylides are reported. The π-sulfuranes employed include phenacylidenedimethylsulfurane, p-fluorophenacylidenedimethylsulfurane, p-chlorophenacylidine-dimethylsulfurane, p-bromophenacylidenedimethylsulfurane, p-nitrophenacylidenedimethylsulfurane and m-nitrophenacylidene-dimethylsulfuranes. The presence of the sulfonium ions non coordinated counter ion was supported by IR spectral data. The ν(C=O) frequencies of the complexes showed blue shift, relative to those of free S-ylides, approaching those of completely protonated 'Onium'salt, which indicates co-ordination via the methine carbon atom. The structures of the resulting complexes were elucidated on the basis of IR spectral data and elemental analysis.

V.2. INTRODUCTION :

Ylides are considered as versatile ligands for metals in their various oxidation states. They differ from other organic ligands in that the ylides co-ordinate to the metal ion as a neutral ligand to form a σ-bond between the ylide carbon and

the metal atom. The work on metallation of ylides was started in the right earnest from 1965[1]. Previous to this, only preliminary studies on the reaction of inorganic components with ylides were reported[2]. Various groups of workers have since been attracted more and more by many fascinating aspects of this newly emerging branch of organometallic chemistry. Lateron many studies have been reported concerning the reaction of various ylides with boron, aluminium[3,4], mercury[5,6] and tin compounds. However, there have been few reports on the reactions of ylide with transitional metals[7-11] and studies of metallate complexes containing co-ordinating ylide are also very rare to-date[10-12].

Recently, studies on the synthesis of metallate complexes by the reaction of pyridinium ylides with metal halides, has attracted a good deal of attention in the field of organometallic chemistry. Based on up-to-date information pyridinium ylides are supposed to hold a superior position among the other nitrogen ylides. Such studies though still in infancy, showed a great potentiality due to marked stability of the resulting ylide metallate complexes.

It is apparent that work in the field of metallation with S-ylide has begun. There is sure promise of great potential for the ylide metallate complexes are charecterised by greater stability than their parent ylide. It is in this context that

it was thought worthwhile to extend this type of studies to prepare metallate complexes of some transtional metals viz. Hg(II),Cd(II),Co(II) and Ni(II) with some p-substitutedn phenacylidenedimethyl sulfonium ylide.

V.3. RESULTS AND DISCUSSION :

Reaction of dimethyl sulfide with phenacyl bromide, p-fluorophenacyl bromide, p-chlorophenacyl bromide, p-bromophenacyl bromide, p-nitrophenacyl bromide and m-nitrophenacyl bromide in benzene at reflux temperature, gave phenacyldimethylsulfonium bromide(1a), p-fluorophenacyldimethylsulfonium bromide (1b), p-chlorophenacyldimethylsulfonium bromide(1c), p-bromophenacyl dimethylsulfonium bromide (1d), p-nitrophenacyldimethylsulfonium bromide (1e) and m-nitrophenacyldimethylsulfonium bromide (1f) respectively in fair to good yields. The structures of sulfonium salts (1a-f) were confirmed comparision of melting point of salt with those reported in literature and spectral data.

The IR spectra of salt (1a-f) showed a charecterstic absorption band due to C-O stretching vibrations in the region 1670-1690 Cm^{-1} for carbonyl group. The diagnostic absorption bands in the region 3300-3000 Cm^{-1} were observed due to C-H stretching vibration of methylene groups attached to S-atom. The NMR spectra of salts (1a-f) showed a singlet at δ 3.00-3.15 due to methyl protons directly attached to sulfonium group. A sharp singlet in the range δ 5.0-5.50 exhibited methylene protons

adjecent to sulfur group ($-CH_2-S^{+}<$). The aromatic protons appeared in the range δ 7.20-8.35.

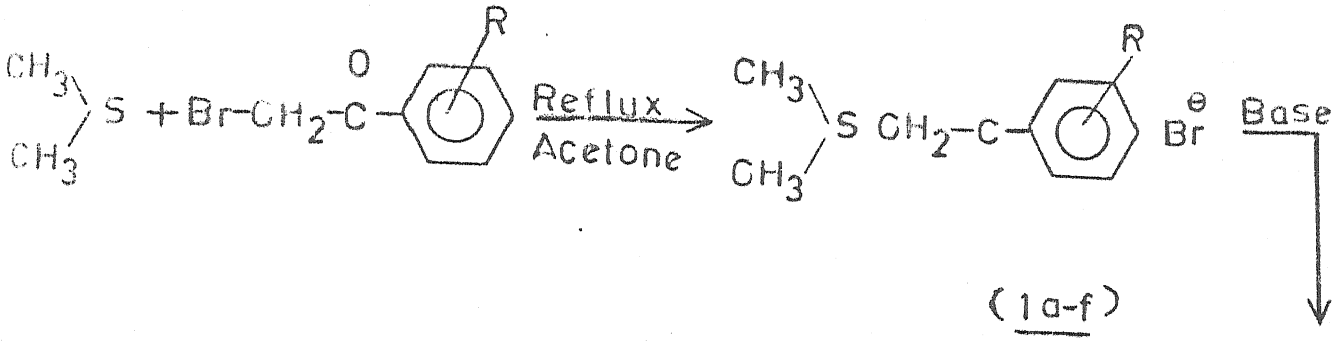
These salts (1a-f) on treatment with aq.NaOH generated a yellow colaration which was changed to orange colour clearly indicating the formation of ylides (2a-f) viz.phenacylidene-dimethyl sulfurane(2a), p-fluorophenacylidenedimethyl sulfurane (2b), p-chlorophenacylidenedimethyl sulfurane (2c), p-bromo-phenacylidenedimethyl sulfurane(2d), p-nitrophenacylidenedimethyl sulfurane (2e) and m-nitrophenacylidenedimethyl sulfurane (2f) in good yields. These ylides (2a-f) were isolated in form of yellowish orange crystals(2a-f) were charecterised on the basis of IR and NMR spectral data. The IR(KBr) spectral data showed a band of medium intensity in region 1500-1530Cm^{-1} due to stretching vibration of C-O bond which is charecterestic absorption of enolate structure. The NMR spectra showed a singlet at 3.05-3.20 due to two methyl protons. A methine proton in ylides (2a-f) was absorbed at δ4.25-4.35. The aromatic protons were exhibited in the region δ7.20-8.15.

The ylide (2a-f) so generated, is isolable but can not be stored for a quite long time owing to its susceptibility towards atmospheric components and therefore the reaction of ylides was carried out in an atmosphere of nitrogen. The sulfonium salt (1a-f) are used in the reaction and ylides (2a-f) was generated in situ from its salts(1a-f).

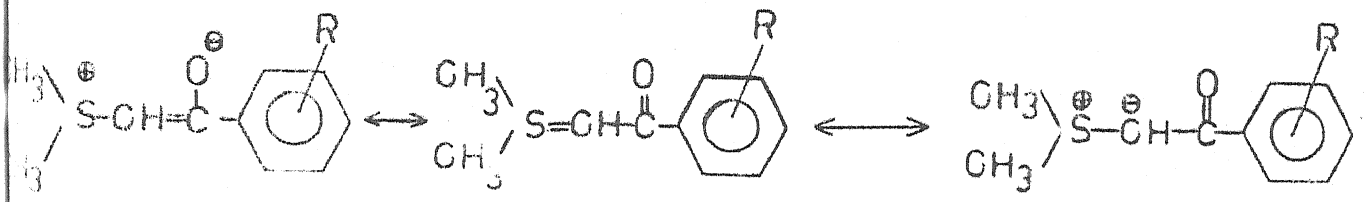
The reaction of ylides (2a-f) with the halides of Hg(II), Cd(II), Co(II) and Ni(II) (MX_2 where M=metal, X=halogen) in methanol gave a series of metal halide complexes (4a-e, 9a-e) in 40-70% yields. The metal halide complexes $[M_2(ylide)_2X_4]$ presumbly contain a bridging $X^{\ominus}$ group electron donating substituted (Cl, Br) having lone pair attached to phencyl ring of ylide counterpart of ylide (2b-d) increase the ease of formation of complex as evidenced by yield of final products (4-a).

The metallation reaction seems to proceed via intermediate ylide carbanion. The ylides used for the reactions may be represented by the three canonical structures (Scheme V.1). The value of carbonyl stretching vibrations observed for the ylides (4-9) showed an important contribution of enolate structure (III). In this structure of lone pair of electrons formally on the ylide carbanion is considered to be delocalised to a large extent. Thus, the ylides have two possible co-ordination sites towards the metal halide carbonyl oxygen which would result in low frequency shift of ν(C=O) owing increased enolate character. In general, the analytical data of the complexes were found to be in fairly good agreement with indicated formulations. But one can not rule out the presence of small amounts of the other salts which might be expected in view of high halide mobility likely to be encountered in these systems. Elemental analysis indicated that the complexes were 1:1 adducts probably dinuclear

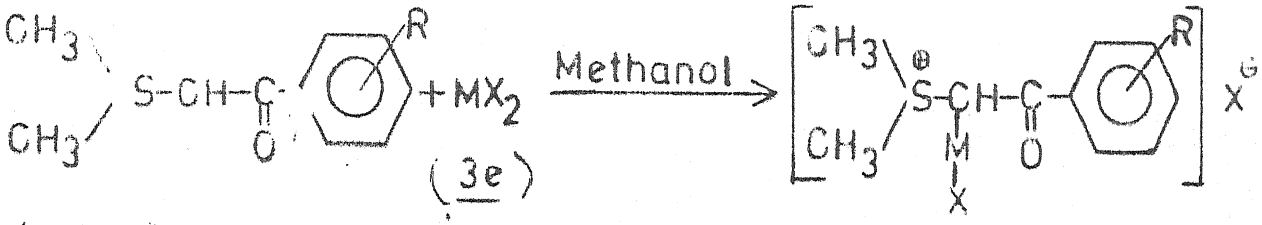
Scheme.V.1



(1a-f)



(2a-f) (2a-f) (2a-f)



(3e)

(2a-f)

(4a-9e)

with halide bridging. The physical and spectral properties are included in table V.1 & V.2.

V.4. EXPERIMENTAL :

V.4.1. Starting Materials :

All the reagents were obtained from commercial sources (E.Merck, BDH,SISCO etc.). Starting materials were prepared according to the procedure reported in literature.

V.4.2. Prepration of p-substituted phenacyldimethyl-sulfonium bromide (1a-f):

General procedure :

A solution of 100m mole of p-substituted phenacyl bromide and 100m mole of dimethylsulfide in 100ml of anhydrous benzene or tetrahydrafuran, was boiled for 6-8hrs. The excess of the solvent was evaporated and petrolium ether was added to precipitate the salts (1a-f) which were, then recrystallized from chloroform, petrolium ether (1:2). This procedure was followed to prepre the following salts-

Phenacyldimethylsulfonium bromide(1a), white crystalline solid, m.p.138-140°C(Lit.[13] m.p.140°C), IR(KBr)data, 1690 Cm^{-1} (νC=O)

NMR($CDCl_3$)data(δ ppm) : 3.15(s,6H,di CH_3),5.05(s,2H,CH_2-S$^+$<) 7.10-8.30(m,5H,ArH).

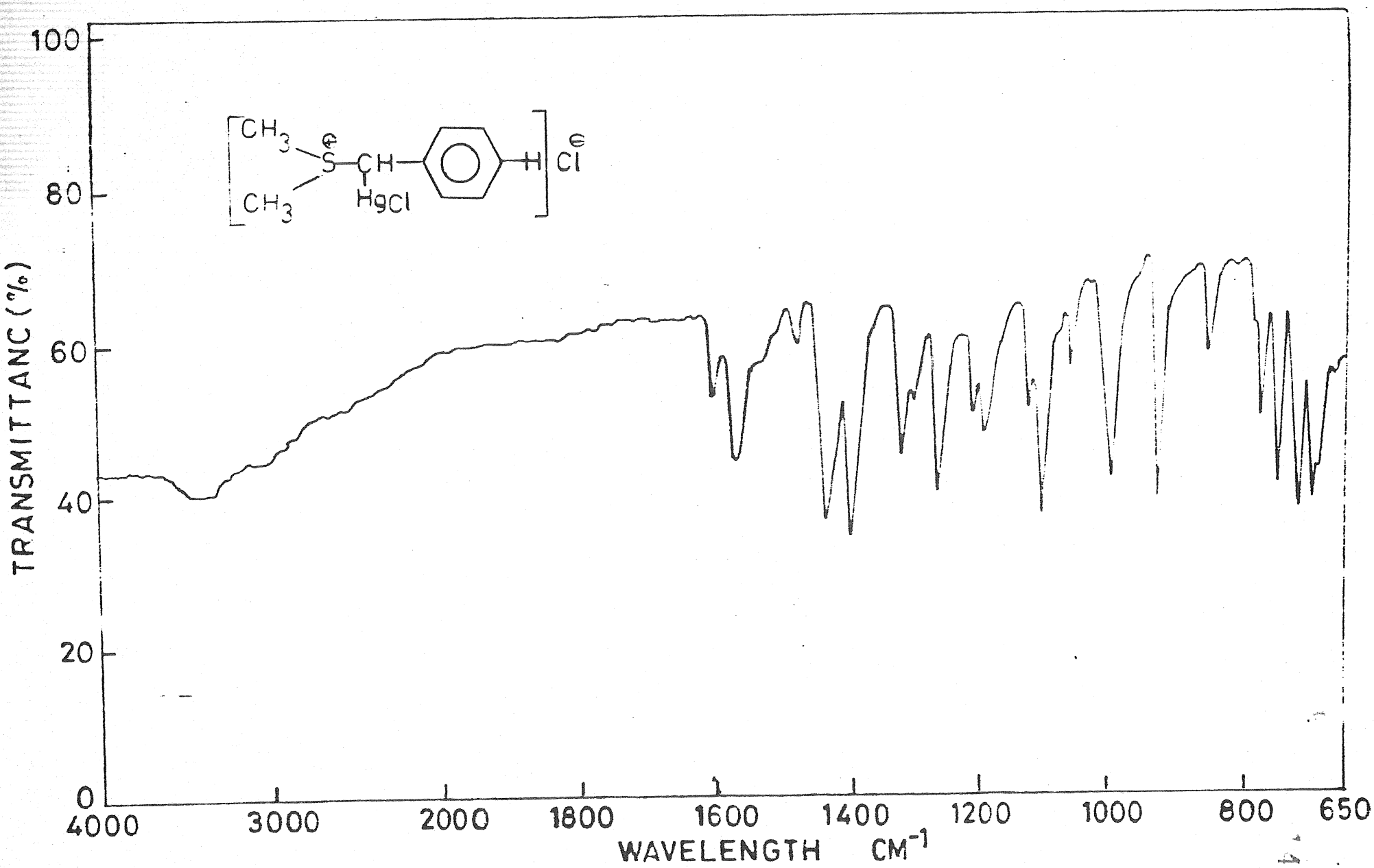


FIG. V.1 IR SPECTRUM OF COMPOUND (4a)

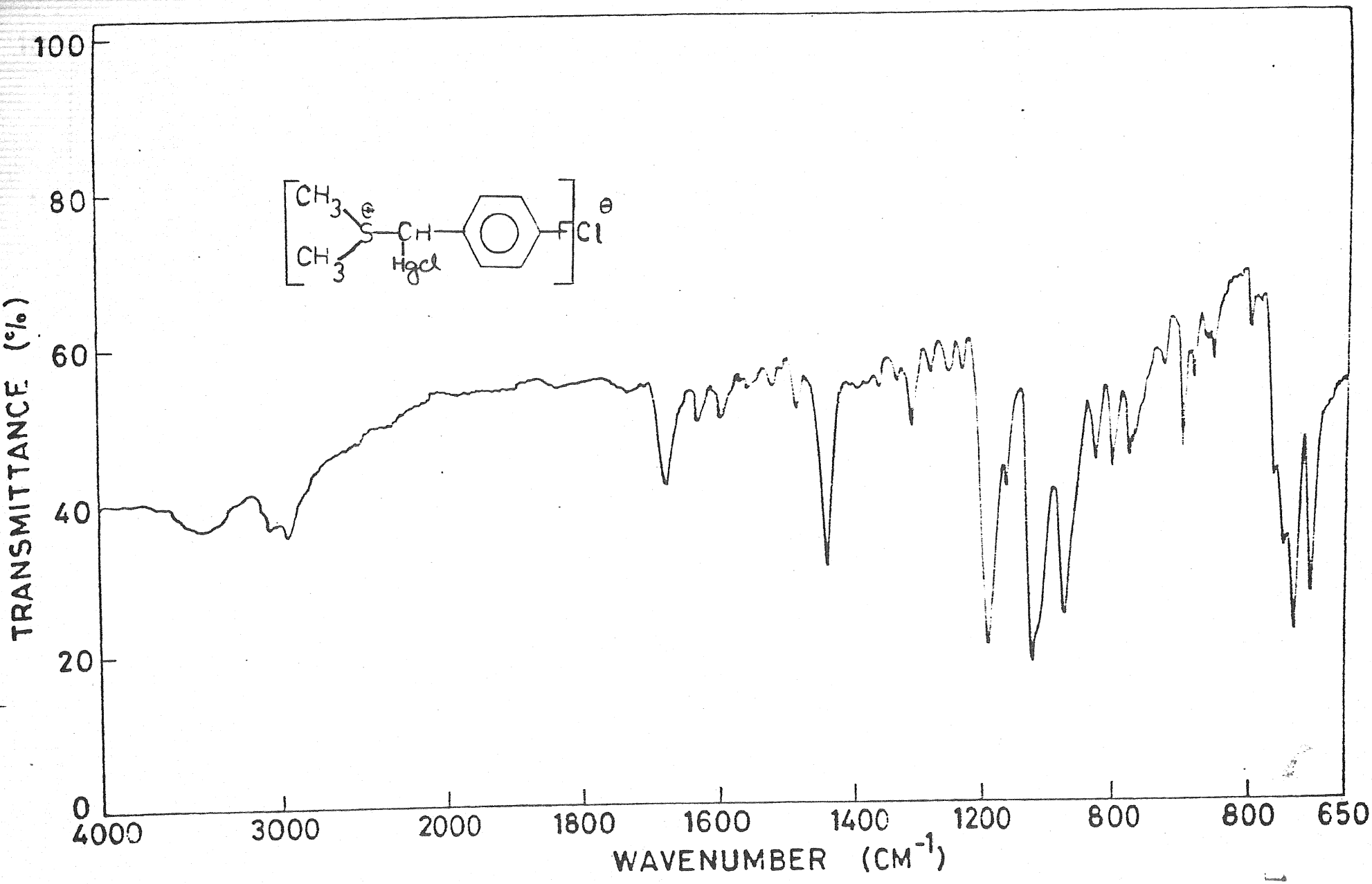


FIG. V.2 IR SPECTRUM OF SALT (5a)

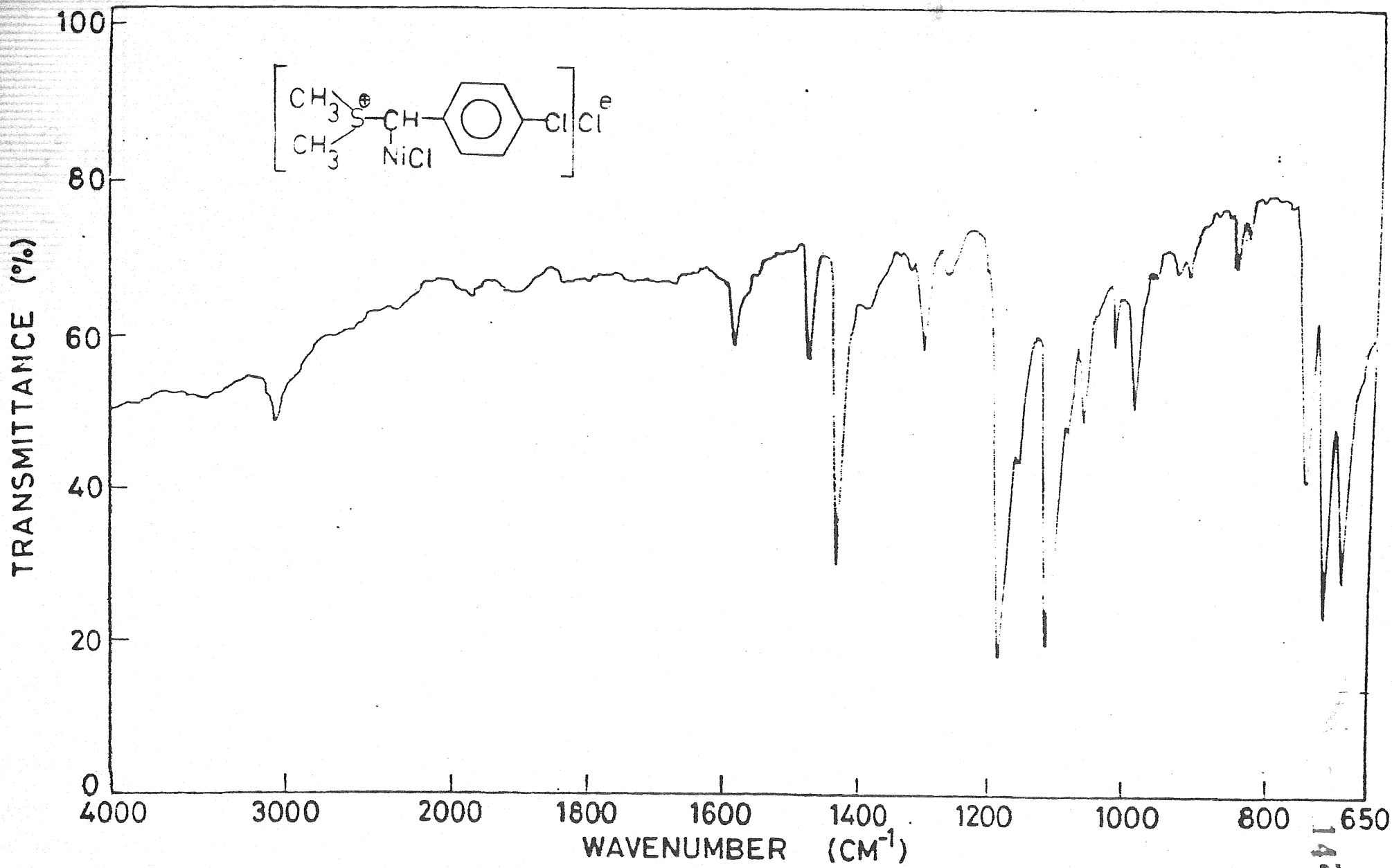


FIG. V.3 IR SPECTRUM OF COMPOUND (6a)

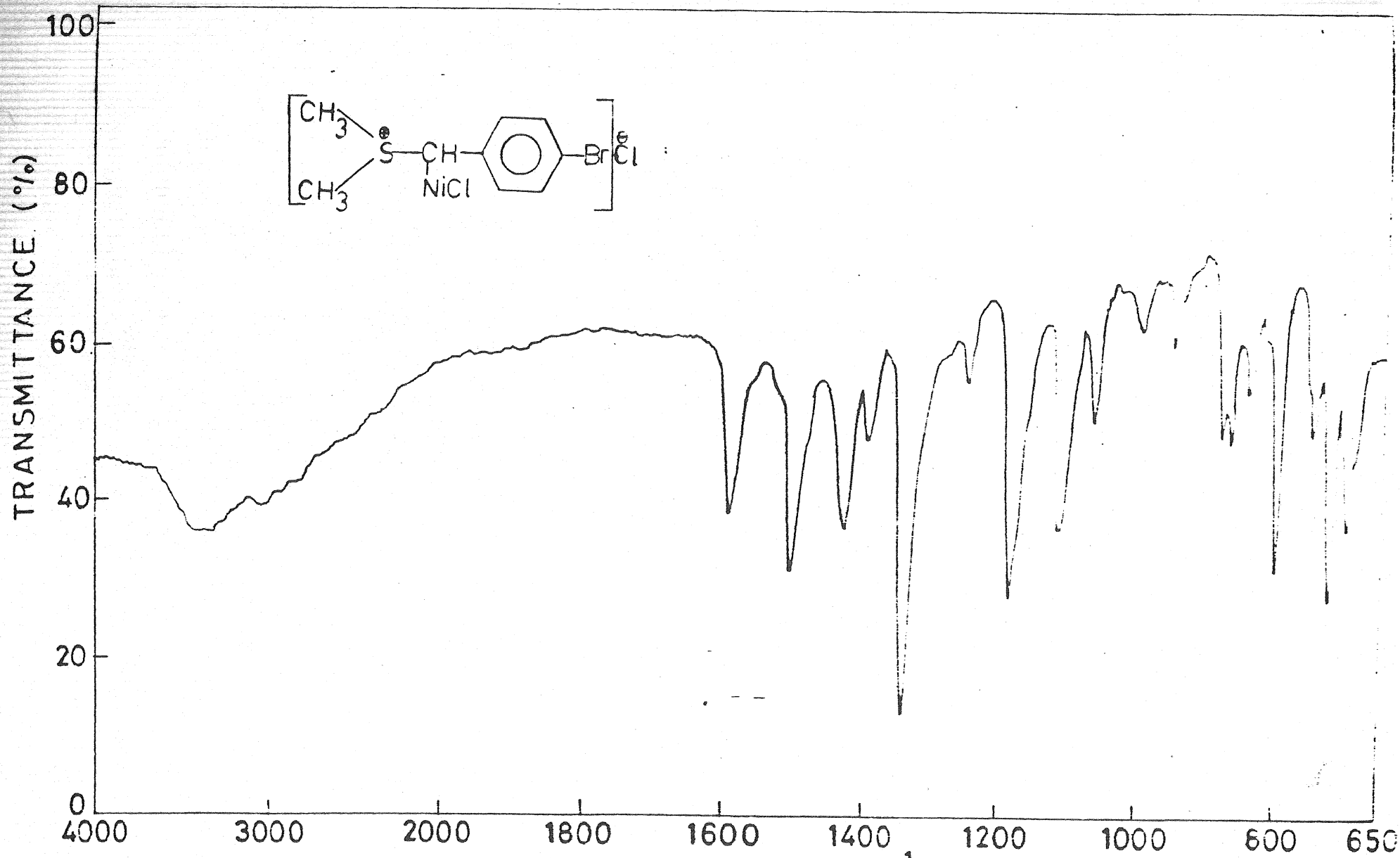


FIG. V·41 R SPECTRUM OF COMPOUND (7a)

ρ-fluorophenacyldimethylsulfonium bromide(1b)

white coloured, m.p.(142-144°C) (Lit.[14] m.p.144-145°C)

IR(KBr) data: 1675 Cm^{-1} (ν C=O)

NMR($CDCl_3$) (δ ppm): 3.25(s,6H,diCH_3); 5.40(s,2H,CH_2);
7.25-7.85(m,4H,ArH).

p-chlorophenacyldimethylsulfonium bromide(1c)

pale yellow crystals, m.p.120-122°C(Lit.[15] m.p.120°C)

IR(KBr) data: 1670 Cm^{-1} (ν C=O)

NMR($CDCl_3$) data(δ ppm): 3.15(s,6H,diCH_3); 5.25(s,2H,-CH_2-S^+<);
7.20-8.25(m,4H,ArH).

p- bromophenacyldimethylsulfonium bromide (1d)

yellow crystals, m.p.132-134°C(Lit.[16] m.p.134°C)

IR(KBr) data: 1685 Cm^{-1} (ν C=O)

NMR($CDCl_3$) data(δ ppm): 3.20(s,6H,diCH_3); 5.15(s,2H,CH_2-S^+<);
7.20-8.25(m,4H,ArH).

p- nitrophenacyldimethylsulfonium bromide (1e)

orange yellow crystals, m.p.150-152°C(Lit.[17] m.p.152-154°C)

IR(KBr) data: 1690 Cm^{-1} (ν C=O)

NMR($CDCl_3$) data(δ ppm): 3.30(s,6H,diCH_3); 5.35(s,2H,CH_2-S^+<);
7.25-8.40(m,4H,ArH).

m- nitrophenacyldimethylsulfonium bromide(1f)

orange(m.p.148-150°C) (Lit.[18] m.p.150°C)

IR(KBr) data: 1685 Cm^{-1} (ν C=O)

NMR($CDCl_3$) data(δ ppm): 3.30(s,6H,diCH_3); 5.10(s,2H,CH_2);
7.15-7.70(m,4H,ArH).

V.4.3. Prepration of p-substituted phenacylidenedimethyl sulfurane (2a-f):

Taking the p-substituted phenacyldimethylsulfonium bromide (50m mole) was dissolved in water (30ml). The coloured suspension was filtered and the clear filterate was treated with 10% Aq.NaOH (15ml). The solution was stirred for 6-8 hrs.and then extracted several times with $CHCl_3$. The chloroform extract was dried with Na_2SO_4 and evaporated to give coloured oil which on cooling gave coloured solid. These coloured solids on crystallization with ethanol afforded light coloured crystals of p-substituted phenacylidene dimethyl sulfurane .

p-phenacylidenedimethylsulfurane (2a)

yellow crystals m.p.70-72°C(Lit. m.p.74-76°C)

IR(KBr)data: 1690Cm^{-1}($\nu C=O$)

NMR($CDCl_3$)data(δppm): 3.15(s,6H,diCH_3), 5.05(s,2H,-$\bar{C}$H-$S^+<$)
7.10-8.30(m,5H,ArH).

p-fluorophenacylidenedimethylsulfurane(2b)

light pale yellow crystals m.p.66-68°C(Lit. m.p.66°C)

IR(KBr)data: 1530Cm^{-1}($\nu C=O$)

NMR($CDCl_3$)data(δppm): 3.20(s,6H,diCH_3); 4.35(s,1H,-$\bar{C}$H-$S^+<$)
7.30-8.20(m,4H,ArH).

p-chlorophenacylidenedimethylsulfurane(2c)

light raddish yellow crystals, m.p.80-82°C(Lit.78-80°C)

IR(KBr)data: 1520Cm^{-1}($\nu C=O$)

NMR($CDCl_3$)data(δ ppm): 3.15(s,6H,diCH_3); 4.20(s,1H,C$\bar{H}$-S^+<); 7.15-8.15(m,4H,ArH).

p-bromophenacylidenedimethylsulfurane(2d)

yellow shining ,m.p. 86-88°C(Lit. m.p.90-91°C)

IR(KBr)data: 1525Cm^{-1}(νC=O)

NMR($CDCl_3$)data(δ ppm): 3.10(s,6H,diCH_3); 4.15(s,1H,C$\bar{H}$-S^+<); 7.20-8.20(m,4H,ArH).

p-nitrophenacylidenedimethylsulfurane(2e)

light reddish violet crystals, m.p.90-92°C(Lit. m.p.92-94°C)

IR(KBr)data: 1530Cm^{-1}(νC=O)

NMR($CDCl_3$)data(δ ppm): 3.30(s,6H,diCH_3); 4.35(s,1H,C$\bar{H}$-S^+<); 7.25-8.25(m,4H,ArH).

m-nitrophenacylidenedimethylsulfurane(2f)

red violet crystals, m.p.98-100°C (Lit. m.p.96-98°C)

IR(KBr)data: 1525Cm^{-1}(νC=O)

NMR($CDCl_3$)data(δ ppm): 3.25(s,6H,diCH_3); 4.30(s,1H,C$\bar{H}$-S^+<); 7.20-8.15(m,4H,ArH).

V.4.4. Synthesis of metal ylide complexes(4a-9e):

General procedure :

A solution of metal halide (1.0m mole) in methanol (20ml) was added dropwise to the solution of substituted phenacylidenedimethylsulfonium ylide(2.0m mole) in methanol (20ml). Immediately after the complete addition a precipitate

began to form rapidly. The mixture was stirred for further two hours at the room temperature and the solid was then filtered off, washed with methanol and diethyl ether and dried vacuo over calcium sulfate to afford titled complexes(4a-9e) in good yields.

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TABLE V.1.: PHYSICAL PROPERTIES OF METAL YLIDE COMPLEXES(4a-9e).

Compound	M	X	R	m.p. ^{o}C	Yields %	Analysis found(Calcd.)% C	H	X =Cl,Br,F
1	2	3	4	5	6	7	8	9
4a	Hg	Cl	H	190-92	40	26.50 (26.54)	2.69 (2.65)	15.91 (15.71)
b	Hg	Br	H	185-87	50	25.90 (25.92)	2.54 (2.59)	17.37 (17.35)
c	Cd	Cl	H	198-20	45	19.51 (19.56)	3.34 (3.31)	19.48 (19.50)
d	Ni	Cl	H	170-72	50	38.98 (38.96)	3.86 (3.89)	23.07 (23.05)
e	Co	Cl	H	180-82	45	38.69 (38.71)	3.86 (3.87)	22.92 (22.90)
5a	Hg	Cl	4-F	205-08	50	25.50 (25.53)	2.35 (2.34)	15.12 (15.11)
b	Hg	Br	4-F	188-90	45	21.49 (21.47)	1.98 (1.96)	28.64 (28.62)
c	Cd	Cl	4-F	168-70	48	31.46 (31.49)	2.88 (2.89)	18.62 (18.64)
d	Ni	Cl	4-F	180-82	50	36.84 (36.81)	3.35 (3.37)	21.79 (21.78)
e	Co	Cl	4-F	178-80	55	36.56 (36.59)	3.37 (3.35)	21.67 (21.65)

Contd. Table V.1.

1	2	3	4	5	6	7	8	9
6a	Hg	Cl	4-Cl	190-92	65	24.65 (24.67)	2.23 (2.26)	21.86 (21.89)
b	Hg	Br	4-Cl	180-82	65	32.02 (32.04)	2.93 (2.94)	9.49 (9.48)
c	Cd	Cl	4-Cl	166-68	55	30.22 (30.19)	3.63 (3.65)	26.80 (26.79)
d	Ni	Cl	4-Cl	172-74	60	35.06 (35.04)	3.22 (3.20)	31.06 (31.09)
e	Co	Cl	4-Cl	164-66	58	34.82 (34.83)	3.20 (3.19)	30.92 (30.91)
7a	Hg	Cl	4-Br	180-82	60	21.75 (21.78)	1.92 (1.99)	12.87 (12.89)
b	Hg	Br	4-Br	170-72	55	19.37 (19.35)	1.75 (1.77)	2.56 (2.58)
c	Cd	Cl	4-Br	202-04	50	27.10 (27.11)	2.48 (2.49)	16.04 (16.06)
d	Ni	Cl	4-Br	210-12	45	30.82 (30.85)	2.81 (2.84)	18.35 (18.35)
e	Co	Cl	4-Br	178-80	50	30.86 (30.84)	2.80 (2.83)	18.23 (18.25)
8a	Hg	Cl	4-NO_2	164-66	40	24.13 (24.14)	2.23 (2.21)	14.30 (14.29)
b	Hg	Br	4-NO_2	186-88	45	23.70 (23.72)	2.15 (2.17)	15.79 (15.81)

Contd. Table V.1.

1	2	3	4	5	6	7	8	9
c	Cd	Cl	4-NO_2	198-20	50	20.39 (20.41)	2.67 (2.69)	17.42 (17.40)
d	Ni	Cl	4-NO_2	190-92	40	33.97 (33.99)	3.14 (3.12)	20.14 (20.11)
e	Co	Cl	4-NO_2	180-82	45	33.89 (33.80)	3.07 (3.09)	20.13 (20.11)
9a	Hg	Cl	3-NO_2	180-82	50	24.25 (24.14)	2.10 (2.21)	4.35 (4.29)
b	Hg	Br	3-NO_2	192-94	45	23.86 (23.72)	2.12 (2.17)	15.74 (15.81)
c	Cd	Cl	3-NO_2	178-80	55	20.50 (20.41)	2.61 (2.69)	17.51 (17.40)
d	Ni	Cl	3-NO_2	200-02	40	33.88 (33.99)	3.19 (3.12)	20.18 (20.11)
e	Co	Cl	3-NO_2	196-98	45	33.75 (33.80)	3.15 (3.09)	20.22 (20.11)

TABLE V.2: IR SPECTRAL DATA FOR METAL COMPLEXES. (4a-9e)

Compound	IR Data (KBr) (Cm^{-1})			
	ν C-H	ν C=O	ν C-M	ν NO_2
4a	3405	1650	730	
b	3380	1680	725	
c	3370	1668	715	
d	3285	1645	740	
e	3400	1640	730	
5a	3490	1630	710	
b	3420	1665	735	
c	3405	1650	715	
d	3385	1660	728	
e	3408	1655	730	
6a	3400	1640	738	
b	3415	1675	730	
c	3408	1680	738	
d	3420	1666	722	
e	3410	1684	732	
7a	3428	1670	718	
b	3408	1668	728	
c	3398	1650	708	
d	3410	1645	715	
e	3402	1650	710	
8a	3420	1645	718	1338,1520
b	3415	1668	728	1320,1515
c	3430	1675	720	1335,1525
d	3408	1667	730	1330,1535
e	3415	1655	720	1338,1540

CONTD. TABLE V.2.

Compound	IR Data (KBr) (Cm^{-1})			
	ν C-H	ν C=O	ν C-M	ν NO_2
9a	3415	1668	735	1320, 1540
b	3395	1655	728	1328, 1538
c	3405	1666	735	1335, 1548
d	3428	1665	745	1330, 1540
e	3420	1675	730	1338, 1545

ν = Stretching vibrations.